

Comprehensive Applied Basic Sciences CABS for MDS Students

As per DCI Syllabus

Questions–Answers

Presented in
Question–Answer
Form for
Quick and Easy
Review of
Basic Subjects

Forewords by
Vimal K Sikri
S Jayachandran

The Book Covers

Human Anatomy, Embryology and Histology

Dental Anatomy and Dental Histology

Physiology

Biochemistry

Microbiology

Pathology

Pharmacology

Biostatistics, Research Methodology and Ethics

Dental Materials

Genetics

Suresh K Sachdeva



CBS Publishers & Distributors Pvt Ltd

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Questions—Answers

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Science and technology are constantly changing fields. New research and experience broaden the scope of information and knowledge. The authors have tried their best in giving information available to them while preparing the material for this book. Although, all efforts have been made to ensure optimum accuracy of the material, yet it is quite possible some errors might have been left uncorrected. The publisher, the printer and the authors will not be held responsible for any inadvertent errors, omissions or inaccuracies.

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Foreword

It is my privilege to write the Foreword to *Comprehensive Applied Basic Sciences (CABS) for MDS Students* by Suresh K Sachdeva. I am pleased to note that the author has written and compiled the entire basic science topics for postgraduate students in one book, which was much needed. This is indeed a very valuable book as it makes the subject easy and comprehensible. The author has been able to put forward the subject in a very simple and straight manner. The book is designed and written in such a way that it is clear, comprehensive yet concise and student-friendly.

The hallmark of this book is that the author has covered all the topics of basic science subjects according to the syllabus prescribed by Dental Council of India for all the specialties of dentistry, making this book as "common to all" MDS students. Also, the previous year's questions from almost all the universities included and have been explained with flowcharts, tables and diagrams for easy learning. I am sure that this book has been compiled to meet the needs of students by covering all the basic science subjects. Dr Sachdeva needs to be complemented for making a special effort to address the examination needs of the postgraduate students. I wish him all the very best in his endeavor.



A stylized handwritten signature in black ink.

Vimal K Sikri

MDS, DOOP (PU), DEME (AIU), FICD

Principal

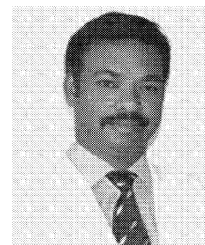
Department of Medical Education and Research, Government of Punjab
Punjab Government Dental College and Hospital
Amritsar

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Foreword

Enthusiasm is the driving force that overcomes all obstacles

It is my proud privilege to write the Foreword to *Comprehensive Applied Basic Sciences for MDS Students* by Suresh K Sachdeva, Associate Professor, Department of Oral Medicine and Radiology, Surendera Dental College and Research Institute, Sri Ganganagar, Rajasthan, on applied basic sciences for postgraduate students. It is a comprehensive, yet concise, and well written text. The strength of the book is centred on its lucid language and contemporary concepts. Going through the book, the reader could additionally focus on the points to remember, reflecting the author's understanding of the students' needs. Dr Sachdeva has undertaken an outstanding job of compiling/editing this text into a valuable resource for each student of postgraduate dentistry. I do congratulate him for bringing out this book successfully.



S. Jayachandran

S. Jayachandran MDS, MAMS, PhD, MBA
Professor and Head

Department of Oral Medicine and Radiology
Tamil Nadu Government Dental College and Hospital
Chennai

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Preface

I have written *Comprehensive Applied Basic Sciences (CABS) for MDS Students* not as an author but as a student. When I was doing my postgraduation, every student used to read multiple books, seminars, articles for the applied basic science paper, which consumed a lot of precious time and create unnecessary stress during exam time. If we do preparations as per the previous year's question papers, some difficult and twisted questions make the situation worse. This lead a strong feeling in me to write a comprehensive book for the applied basic sciences which contains all the subjects as solved question-answers, from all over India. I have tried my best to bring out a book which can invoke interest in students in this subject. The basic aim of writing this book is to make the students familiar with the usually asked questions and to give a clear picture of an answer to be written in a particular question.

This book holds the potential of filling the gap that has been felt by dental postgraduate students for years. This book provides the readers a comprehensive and concise overview of the basic science subjects with ten chapters, each having the previous years' questions with answers from almost all the universities of India, arranged as per the syllabus prescribed by Dental Council of India.

The questions are answered as short notes, long questions with "to the point" answers. Also the variants of a question asked in different universities have also been added. Moreover, the answers are selected from the standard textbooks which are usually used by students, to avoid any confusion. And where the answers have been taken from the articles, proper citation of the reference has been given.

This book is written to bring out a concise, easily understandable resource for students to learn and guide them to write well structured answers in their examinations.

I hope that the book will fulfill the need of the students by giving them relevant guidance during their preparation for examination. I am confident that the readers will be greatly benefited by my effort.

I have tried my best to cover all the aspect of applied basic sciences as per the DCI syllabus in my book. As no one is perfect, I humbly accept my limitations regarding shortcomings in the book and I sincerely welcome the constructive suggestions from the readers of this book at cabsformds@rediffmail.com

Suresh K Sachdeva

Acknowledgments

To author a book on my name had been a long awaited dream for me for the last many years. First of all, I thank Almighty for giving me strength and knowledge to write a book even during my hardship period.

My parents deserves my heartfelt acknowledgment for all their encouragement and support during my studies and even thereafter.

I wish to express my sincere gratitude to my esteemed teachers from the Department of Oral Medicine and Radiology, Tamil Nadu Government Dental College and Hospital (my Alma mater), Chennai, for teaching me the fundamentals and polishing my skills, making me what I am today.

I appreciate the support and encouragement received from the Director-Principal, Dr Yogesh Kumar Gupta and Dr S Sunder Raj, Head, Department of Oral Medicine and Radiology, Surendera Dental College and Research Institute, Sri Ganganagar, Rajasthan.

I would like to extend my special thanks and sincere regards to Dr Vimal K Sikri and Dr S Jayachandran for writing the foreword.

I am thankful to my seniors and friends, Dr Shekhar Kapoor, Dr Siddharth Kumar Singh, Dr Manas Gupta, Dr Atul Kaushik, Dr Hari Krishan Yadav, and Dr Ankit Sikri for their whole hearted support and encouragement.

My patients offered me a chance to learn as well as to apply my knowledge on them. My students were always an inspiration. They created a great deal of enthusiasm in me as teacher.

Last but not the least, I am greatly indebted to Mr Satish Kumar Jain (CMD), Mr YN Arjuna (Senior Vice-President) for showing trust in me, providing an opportunity to fulfill my dream. I also need to say thanks to the entire staff of CBS Publishers and Distributors for patiently answering all my queries and making this title published.

Suresh K Sachdeva

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DENTAL COUNCIL OF INDIA SYLLABUS FOR MDS—APPLIED BASIC SCIENCES

DENTAL COUNCIL OF INDIA

(Ministry of Health and Family Welfare, Govt. of India)

SYLLABUS FOR POSTGRADUATE (MDS)

Applied Basic Sciences: The MDS Course in Applied Basic Sciences shall vary according to the particular specialty, similarly the candidates shall also acquire adequate knowledge in other subjects related to their respective specialty.

Applied Basic Sciences optional subjects: (i) Applied Anatomy, (ii) Applied Physiology, (iii) Applied Pathology

Subjects related to different specialties:

1. Biostatistics.
2. Nutrition and Dietetics.
3. Teaching and Testing Methodology.
4. Research Methodology.
5. Psychology and Practice Management.
6. Comparative Anatomy.
7. Genetics Growth and Development.
8. Applied Chemistry including Metallurgy, Dental Materials.

1. PROSTHODONTICS AND CROWN AND BRIDGE

APPLIED ANATOMY OF HEAD AND NECK

General Human Anatomy—Gross Anatomy, Anatomy of Head and Neck in detail. Cranial and facial bones, TMJ and function, muscles of mastication and facial expression, muscles of neck and back including muscles of deglutition and tongue, arterial supply and venous drainage of the head and neck, anatomy of the paranasal sinuses with relation to the Vth cranial nerve. General consideration of the structure and function of the brain. Brief considerations of V, VII, XI, XII, cranial nerves and autonomic nervous system of the head and neck. The salivary glands, pharynx, larynx trachea, esophagus, functional anatomy of mastication, deglutition, speech, respiration, and circulation, teeth eruption, morphology, occlusion and function. Anatomy of TMJ, its movements and myofascial pain dysfunction syndrome.

Embryology: Development of the face, tongue, jaws, TMJ, Paranasal sinuses, pharynx, larynx, trachea, esophagus, Salivary glands, Development of oral and Para oral tissue including detailed aspects of tooth and dental hard tissue formation.

Growth and Development: Facial form and facial growth and development overview of dentofacial growth process and physiology from fetal period to maturity and old age, comprehensive study of craniofacial biology. General physical growth, functional and anatomical aspects of the head, changes in craniofacial skeletal, relationship between development of the dentition and facial growth.

Dental Anatomy: Anatomy of primary and secondary dentition, concept of occlusion, mechanism of articulation, and masticatory function. Detailed structural and functional study of the oral dental and paraoral tissues. Normal occlusion, development of occlusion in deciduous mixed and permanent dentitions, root length, root configuration, tooth-numbering system.

Histology: Histology of enamel, dentin, cementum, periodontal ligament and alveolar bone, pulpal anatomy, histology and biological consideration. Salivary glands and histology of epithelial tissues including glands. Histology of general and specific connective tissue including bone, hematopoietic system, lymphoid, etc.

Muscle and neural tissues, endocrinal system including thyroid, salivary glands, histology of skin, oral mucosa, respiratory mucosa, connective tissue, bone, cartilage, cellular elements of blood vessels, blood, lymphatic, nerves, muscles, tongue, tooth and its surrounding structures.

Anthropology and evolution: Comparative study of tooth, joints, jaws, muscles of mastication and facial expression, tongue, palate, facial profile and facial skeletal system. Comparative anatomy of skull, bone,

brain, musculoskeletal system, neuromuscular coordination, posture and gait.

Applied genetics and heredity: Principles of orofacial genetics, molecular basis of genetics, genetic risks, counseling, bioethics and relationship to orthodontic management. Dentofacial anomalies, Anatomical, psychological and pathological characteristic of major groups of developmental defects of the orofacial structures.

Cell biology: Detailed study of the structure and function of the mammalian cell with special emphasis on ultrastructural features and molecular aspects. Detailed consideration of intercellular junctions. Cell cycle and division, cell-to-cell and cell—extracellular matrix interactions.

APPLIED PHYSIOLOGY AND NUTRITION

Introduction, mastication, deglutition, digestion and assimilation, Homeostasis, fluid and electrolyte balance. Blood composition, volume, function, blood groups and hemorrhage. Blood transfusion, circulation, heart, pulse, blood pressure, capillary and lymphatic circulation, shock, respiration, control, anoxia, hypoxia, asphyxia, artificial respiration. Endocrine glands in particular reference to pituitary, parathyroid and thyroid glands and sex hormones. Role of calcium and vit D in growth and development of teeth, bone and jaws. Role of vit. A, C and B complex in oral mucosal and periodontal health. Physiology and function of the masticatory system. Speech mechanism, mastication, swallowing and deglutition mechanism, salivary glands and Saliva

Endocrines: General principles of endocrine activity and disorders relating to pituitary, thyroid, pancreas, parathyroid, adrenals, gonads, including pregnancy and lactation. Physiology of saliva, urine formation, normal and abnormal constituents; Physiology of pain, Sympathetic and parasympathetic nervous system. Neuromuscular co-ordination of the stomatognathic system.

APPLIED NUTRITION

General principles, balanced diet, effect of dietary deficiencies and starvation; Diet, digestion, absorption, transportation and utilization, diet for elderly patients.

Applied biochemistry: General principles governing the various biological activities of the body, such as osmotic pressure, electrolytic dissociation, oxidation-reduction, etc. general composition of the body, intermediary metabolism, Carbohydrates, proteins, liquids and their metabolism; Enzymes; Vitamins and minerals; Hormones; Blood and other body fluids; Metabolism of inorganic elements; Detoxication in the body; Antimetabolites.

APPLIED PHARMACOLOGY AND THERAPEUTICS

Definition of terminologies used: Dosage and mode of administration of drugs. Action and fate of drugs in the body: Drug addiction, tolerance and hypersensitive reactions: Drugs acting on the central nervous system, general anesthetics hypnotics. Analeptics and tranquilizers; Local anesthetics; Chemotherapeutics and antibiotics; Antitubercular and antisyphilitic drugs; Analgesics and antipyretics; Antiseptics, styptics; Sialogogues and antisialogogues; Hematinics; Cortisone, ACTH, insulin and other antidiabetics vitamins: A, D, B-complex group C and K, etc. Chemotherapy and radiotherapy.

APPLIED PATHOLOGY

Inflammation, repair and degeneration; Necrosis and gangrene, Circulatory disturbances; Ischemia, hyperemia, chronic venous congestion, edema, thrombosis, embolism and infarction. Infection and infective granulomas; Allergy and hypersensitive reaction; Neoplasm; Classification of tumors; Carcinogenesis, characteristics of benign and malignant tumors, spread of tumors. Applied histopathology and clinical pathology.

APPLIED MICROBIOLOGY

Immunity, knowledge of organisms commonly associated with diseases of the oral cavity (morphology cultural characteristics, etc.) of strepto-, staphylo-, pneumo-, gono-, and meningococci; Clostridia group of

organisms; Spirochetes, organisms of tuberculosis, leprosy, diphtheria, actinomycosis and moniliasis, etc. Virology; Cross infection control, sterilization and hospital waste management.

- a. **Applied Oral Pathology:** Developmental disturbances of oral and paraoral structures; Regressive changes of teeth; Bacterial, viral and mycotic infections of oral cavity; Dental caries, diseases of pulp and periapical tissues; Physical and chemical injuries of the oral cavity, oral manifestations of metabolic and endocrine disturbances; Diseases of the blood and blood forming organism in relation to the oral cavity; Periodontal diseases; Diseases of the skin, nerves and muscles in relation to the oral cavity.
- b. **Laboratory Determinations:** Blood groups, blood matching, RBC and WBC count; Bleeding and clotting time; Smears and cultures—urine analysis and culture.

Biostatistics: Study of biostatistics as applied to dentistry and research. Definition, aim characteristics and limitations of statistics, planning of statistical experiments, sampling, collection, classification and presentation of data (tables, graphs, pictograms, etc.); Analysis of data.

INTRODUCTION TO BIOSTATISTICS

Scope and need for statistical application to biological data. Definition of selected terms—scale of measurements related to statistics; Methods of collecting data, presentation of the statistical diagrams and graphs. Frequency curves, mean, mode of median; Standard deviation and coefficient of variation; Correlation: Co-efficient and its significance; Binominal distributions, normal distribution and Poisson distribution; Tests of significance.

RESEARCH METHODOLOGY

Understanding and evaluating dental research, scientific method and the behavior of scientists, understanding to logic—inductive logic—analogy, models, authority, hypothesis and causation; Quacks; Cranks; Abuses of logic; Measurement and errors of measurement, presentation of results; Reliability, sensitivity and specificity diagnosis test and measurement; Research strategies; Observation; Correlation; Experimentation and experimental design. Logic of statistical interference balance judgements, judgement under uncertainty, clinical vs scientific judgement, problem with clinical judgement, forming scientific judgements, the problem of contradictory evidence, citation analysis as a means of literature evaluation, influencing judgement: Lower forms of rhetorical life; Denigration; Terminal; Inexactitude.

APPLIED RADIOLOGY

Introduction, radiation, background of radiation, sources, radiation biology, somatic damage, genetic damage, protection from primary and secondary radiation; Principles of X-ray production; Applied principles of radiotherapy and aftercare.

ROENTGENOGRAPHIC TECHNIQUES

Intraoral: Extraoral roentgenography; Methods of localization digital radiology and ultrasound; Normal anatomical landmarks of teeth and jaws in radiograms, temporomandibular joint radiograms, neck radiograms.

APPLIED MEDICINE

Systemic diseases and its influence on general health and oral and dental health. Medical emergencies in the dental offices: Prevention, preparation, medicolegal consideration, unconsciousness, respiratory distress, altered consciousness, seizures, drug related emergencies, chest pain, cardiac arrest, premedication, and management of ambulatory patients, resuscitation, applied psychiatry, child, adult and senior citizens. Assessment of case, premedication, inhibition, monitoring, extubation, complication assist in OT for anesthesia.

APPLIED SURGERY AND ANESTHESIA

General principles of surgery, wound healing, incision wound care, hospital care, control of hemorrhage, electrolyte balance. Common bandages, sutures, splints, shifting of critically ill patients, prophylactic therapy, bone surgeries, grafts, etc. surgical techniques, nursing assistance, anesthetic assistance. Principles in speech therapy, surgical

and radiological craniofacial oncology, applied surgical ENT and ophthalmology.

PLASTIC SURGERY

Applied understanding and assistance in programmes of plastic surgery for prosthodontics therapy.

APPLIED DENTAL MATERIAL

- All materials used for treatment of craniofacial disorders: Clinical, treatment, and laboratory materials; Associated materials; Technical consideration, shelf life, storage, manipulations, sterilization, and waste management.
- Students shall be trained and practiced for all clinical procedures with an advanced knowledge of theory of principles, concepts and techniques of various honorably accepted methods and materials for prosthodontics, treatment modalities includes honorable accepted methods of diagnosis, treatment plan, records maintenance, and treatment and laboratory procedures and aftercare and preventive.
- Understanding all applied aspects for achieving physical, psychological wellbeing of the patients for control of diseases and/or treatment related syndromes with the patient satisfaction and restoring function of craniomandibular system for a quality of life of a patient.
- The theoretical knowledge and clinical practice shall include principles involved for support, retention, stability, esthetics, phonation, mastication, occlusion, behavioral, psychological, preventive and social aspects of science of prosthodontics including Crown and bridge and implantology.
- Theoretical knowledge and clinical practice shall include knowledge for laboratory practice and material science. Students shall acquire knowledge and practice of history taking, systemic and oro- and Craniofacial region and diagnosis and treatment plan and prognosis record maintaining. A comprehensive rehabilitation concept with pre-prosthetic treatment plan including surgical reevaluation and prosthodontic treatment plan, impressions, jaw relations, utility of face bow and articulators, selection and positioning of teeth for retention, stability, esthetics, phonation and psychological comfort. Fit and insertion and instruction for patients after care and preventive Prosthodontics, management of failed restorations.
- TMJ syndromes, occlusion rehabilitation and craniofacial esthetics. State-of-the art clinical methods and materials for implants supported extra oral and intraoral prosthesis.
- Student shall acquire knowledge of testing biological, mechanical and other physical property of all material used for the clinical and laboratory procedures in prosthodontic therapy.
- Students shall acquire full knowledge and practice. Equipment, instruments, materials, and laboratory procedures at a higher competence with accepted methods.
- All clinical practice shall involve personal and social obligation of cross infection control, sterilization and waste management.

2. PERIODONTOLOGY

APPLIED ANATOMY

1. Development of the periodontium
2. Micro and macrostructural anatomy and biology of the periodontal tissues.
3. Age changes in the periodontal tissues
4. Anatomy of the periodontium
 - Macroscopic and microscopic anatomy
 - Blood supply of the periodontium
 - Lymphatic system of the periodontium
 - Nerves of the periodontium
5. Temporomandibular joint, maxillae and mandible
6. Nerves of periodontics
7. Tongue, oropharynx
8. Muscles of mastication

PHYSIOLOGY

1. Blood
2. Respiratory system: Acknowledge of the respiratory diseases which are a cause of periodontal diseases (periodontal Medicine)
3. Cardiovascular system
 - a. Blood pressure
 - b. Normal ECG
 - c. Shock
4. Endocrinology—hormonal influences on Periodontium
5. Gastrointestinal system
 - a. Salivary secretion—composition, function and regulation
 - b. Reproductive physiology
 - c. Hormones—Actions and regulations, role in periodontal disease
 - d. Family planning methods
6. Nervous system
 - a. Pain pathways
 - b. Taste: Taste buds, primary taste sensation and pathways for sensation.

BIOCHEMISTRY

1. Basics of carbohydrates, lipids, proteins, vitamins, enzymes and minerals.
2. Diet and nutrition and periodontium
3. Biochemical tests and their significance
4. Calcium and phosphorus.

PATHOLOGY

1. Cell structure and metabolism
2. Inflammation and repair, necrosis and degeneration
3. Immunity and hypersensitivity
4. Circulatory disturbances—edema, hemorrhage, shock, thrombosis, embolism, infarction and hypertension
5. Disturbances of nutrition
6. Diabetes mellitus
7. Cellular growth and differentiation, regulation
8. Lab investigations
9. Blood

MICROBIOLOGY

1. General bacteriology
 - a. Identification of bacteria
 - b. Culture media and methods
 - c. Sterilization and disinfection
2. Immunology and infection
3. Systemic bacteriology with special emphasis on oral microbiology—staphylococci, genus *Actinomyces* and other filamentous bacteria and *Actinobacillus actinomycetemcomitans*.
4. Virology
 - a. General properties of viruses
 - b. Herpes, hepatitis, virus, HIV virus
5. Mycology
 - Candidiasis
6. Applied microbiology
7. Diagnostic microbiology and immunology, hospital infections and management.

PHARMACOLOGY

1. General pharmacology
 - a. Definitions: Pharmacokinetics with clinical applications, routes of administration including local drug delivery in periodontics
 - b. Adverse drug reactions and drug interactions.
2. Detailed pharmacology of
 - a. Analgesics—opiod and nonopiod
 - b. Local anesthetics
 - c. Haematinics and coagulants, anticoagulants
 - d. Vit D and calcium preparations
 - e. Antidiabetics drugs

- f. Steroids
 - g. Antibiotics
 - h. Antihypertensive
 - i. Immunosuppressive drugs and their effects on oral tissues
 - j. Antiepileptic drugs
3. Brief pharmacology, dental use and adverse effects of
 - a. General anesthetics
 - b. Antipsychotics
 - c. Antidepressants
 - d. Anxiolytic drugs
 - e. Sedatives
 - f. Antiepileptics
 - g. Antihypertensives
 - h. Antianginal drugs
 - i. Diuretics
 - j. Hormones
 - k. Pre-anesthetic medications
 4. Drugs used in bronchial asthma cough
 5. Drug therapy of
 - a. Emergencies
 - b. Seizures
 - c. Anaphylaxis
 - d. Bleeding
 - e. Shock
 - f. Diabetic ketoacidosis
 - g. Acute addisonian crisis
 6. Dental Pharmacology
 - a. Antiseptics
 - b. Astringents
 - c. Sialogogues
 - d. Disclosing agents
 - e. Antiplaque agents
 7. Fluoride pharmacology

BIOSTATISTICS

- Introduction, definition and branches of biostatistics
- Collection of data, sampling, types, bias and errors
- Compiling data—graphs and charts
- Measures of central tendency (mean, median and mode), standard deviation and variability
- Tests of significance (chi square test, 't' test and Z-test)
- Null hypothesis

ETIOPATHOGENESIS

1. Classification of periodontal diseases and conditions
2. Epidemiology of gingival and periodontal diseases
3. Defense mechanisms of gingiva
4. Periodontal microbiology
5. Basic concepts of inflammation and immunity
6. Microbial interactions with the host in periodontal diseases
7. Pathogenesis of plaque associated periodontal diseases
8. Dental calculus
9. Role of iatrogenic and other local factors
10. Genetic factors associated with periodontal diseases
11. Influence of systemic diseases and disorders of the periodontium
12. Role of environmental factors in the etiology of periodontal disease
13. Stress and periodontal diseases
14. Occlusion and periodontal diseases
15. Smoking and tobacco in the etiology of periodontal diseases
16. AIDS and periodontium
17. Periodontal medicine
18. Dentinal hypersensitivity.

3. ORAL AND MAXILLOFACIAL SURGERY**COURSE CONTENTS**

The program outline addresses both the knowledge needed in oral and maxillofacial Surgery and allied medical specialties in its scope. A minimum of three years of formal training through a graded system of education as specified will equip the trainee with skill and knowledge at its completion to be able to practice basic oral and maxillofacial surgery competently and have the ability to intelligently pursue further apprenticeship towards advanced maxillofacial surgery. The topics are considered as under:

- Basic sciences
- Oral and maxillofacial surgery
- Allied specialties

APPLIED BASIC SCIENCES

A thorough knowledge both on theory and principles in general and particularly the basic medical subjects as relevant to the practice of maxillofacial surgery. It is desirable to have adequate knowledge in biostatistics; Epidemiology, research methodology, nutrition and computers.

ANATOMY

Development of face, paranasal sinuses and associated structures and their anomalies; surgical anatomy of scalp temple and face, anatomy and its applied aspects of triangles of neck, deep structures of neck, cranial and facial bones and its surrounding soft tissues, cranial nerves tongue, temporal and infratemporal region, orbits and its contents, muscles of face and neck, paranasal sinuses, eyelids and nasal septum, teeth, gums and palate, salivary glands, pharynx, thyroid and parathyroid glands, larynx, trachea and esophagus, congenital abnormality of orofacial regions. General consideration of the structure and function of brain and applied anatomy of intracranial venous sinuses; Cavernous sinus and superior sagittal sinus. Brief consideration of autonomous nervous system of head and neck. Functional anatomy of mastication, deglutition, speech, respiration and circulation. Histology of skin, oral mucosa, connective tissue bone, cartilage cellular elements of blood vessels, lymphatic, nerves, muscles, tongue, tooth and its surrounding structures.

PHYSIOLOGY

Nervous system—physiology of nerve conduction, pain pathway, sympathetic and parasympathetic nervous system, hypothalamus and mechanism of controlling body temperature; Blood—its composition hemostasis, blood dyscrasias and its management, hemorrhage and its control, blood grouping, cross matching, blood component therapy, complications of blood transfusion, blood substitutes, autotransfusion, cell savers; Digestive system composition and functions of saliva mastication deglutition, digestion, assimilation, urine formation, normal and abnormal constituents; Respiration control of ventilation anoxia, asphyxia, artificial respiration, hypoxia—types and management; CVS—cardiac cycle, shock, heart sounds, blood pressure, hypertension; Endocrinology—metabolism of calcium; endocrinal activity and disorder relating to thyroid gland, parathyroid gland, adrenal gland, pituitary gland, pancreas and gonads; Nutrition—general principles balanced diet. Effect of dietary deficiency, protein energy malnutrition; Kwashiorkor; Marasmus; Nutritional assessment, metabolic responses to stress, need for nutritional support, enteral nutrition, routes of access to GI tract; Parenteral nutrition, Access to central veins, Nutritional support; Fluid and electrolytic balance/acid–base metabolism—body fluid compartment, metabolism of water and electrolytes, factors maintaining hemostasis, causes and treatment of acidosis and alkalosis.

BIOCHEMISTRY

General principles governing the various biological principles of the body, such as osmotic pressure, electrolytes, dissociation, oxidation, reduction, etc. general composition of body, intermediary metabolism, carbohydrate, proteins, lipids, enzymes, vitamins, minerals and antimetabolites.

GENERAL PATHOLOGY

Inflammation: Acute and chronic inflammation, repair and regeneration, necrosis and gangrene, role of component system in acute inflammation, role of arachidonic acid and its metabolites in acute inflammation, growth factors in acute inflammation role of NSAIDS in inflammation, cellular changes in radiation injury and its manifestation; Wound management: Wound healing factors influencing healing; Properties of suture materials, appropriate uses of sutures; Hemostasis – role of endothelium in thrombogenesis; Arterial and venous thrombi, disseminated intravascular coagulation; Hypersensitivity; Shock and pulmonary failure: Types of shock, diagnosis, resuscitation, pharmacological support, ARDS and its causes and prevention, ventilation and support; Neoplasm—classification of tumors; Carcinogens and carcinogenesis, grading and staging of tumors, various laboratory investigation.

GENERAL MICROBIOLOGY

Immunity, hepatitis B and its prophylaxis, Knowledge of organisms, commonly associated with diseases of oral cavity, culture and sensitivity tests, various staining techniques: Smears and cultures, urine analysis and culture.

ORAL PATHOLOGY AND MICROBIOLOGY

Developmental disturbances of oral and paraoral structures, regressive changes of teeth, bacterial, viral, mycotic infection of oral cavity; Dental caries, diseases of pulp and periapical tissues, physical and chemical injuries of oral cavity, wide range of pathological lesions of hard and soft tissues of the orofacial regions like cysts, odontogenic infection, benign and malignant neoplasms, salivary gland diseases, maxillary sinus diseases, mucosal diseases, oral aspects of various systemic diseases and role of laboratory investigation in oral surgery.

PHARMACOLOGY AND THERAPEUTICS

Definition of terminology used, pharmacokinetics and pharmacodynamic dosage and mode of administration of drugs, action and fate in the body, drug addiction, tolerance and hypersensitivity reactions, drugs acting on CNS, general and local anesthetics, antibiotics and analgesics, antiseptics, antitubercular, sialogogues, hematinics, anti diabetic, Vitamins A, C, D, E, K and B-complex.

COMPUTER SCIENCE

Use of computers in surgery, components of computer and its use in practice, principles of word processing, spreadsheet function database and presentations; the internet and its use. The value of computer based systems in biomedical equipment.

4. ORAL AND MAXILLOFACIAL SURGERY

Applied Anatomy, Physiology, Biochemistry, General and Oral Pathology and Microbiology and Pharmacology.

APPLIED ANATOMY

1. Surgical anatomy of the scalp, temple and face
2. Anatomy of the triangles of neck and deep structures of the neck
3. Cranial and facial bones and its surrounding soft tissues with its applied aspects in maxillofacial injuries.
4. Muscles of head and neck
5. Arterial supply, venous drainage and lymphatics of head and neck
6. Congenital abnormalities of the head and neck
7. Surgical anatomy of the cranial nerves
8. Anatomy of the tongue and its applied aspects
9. Surgical anatomy of the temporal and infratemporal regions
10. Anatomy and its applied aspects of salivary glands, pharynx, thyroid and parathyroid gland, larynx, trachea esophagus
11. Tooth eruption, morphology, and occlusion.
12. Surgical anatomy of the nose.
13. The structure and function of the brain including surgical anatomy of intracranial venous sinuses.
14. Autonomous nervous system of head and neck
15. Functional anatomy of mastication, deglutition, speech, respiration and circulation.
16. Development of face, paranasal sinuses and associated structures and their anomalies
17. TMJ: Surgical anatomy and function

PHYSIOLOGY

1. Nervous system
 - Physiology of nerve conduction, pain pathway, sympathetic and parasympathetic nervous system, hypothalamus and mechanism of controlling body temperature.
2. Blood
 - Composition
 - Hemostasis, various blood dyscrasias and management of patients with the same
 - Hemorrhage and its control

- Capillary and lymphatic circulation.
 - Blood grouping, transfusing procedures.
- 3. Digestive system**
- Saliva—composition and functions of saliva
 - Mastication, deglutition, digestion, assimilation.
 - Urine formation, normal and abnormal constituents.
- 4. Respiration**
- Control of ventilation, anoxia, asphyxia, artificial respiration
 - Hypoxia—types and management
- 5. Cardiovascular system**
- Cardiac cycle
 - Shock
 - Heart sounds
 - Blood pressure
 - Hypertension.
- 6. Endocrinology**
- General endocrinal activity and disorder relating to thyroid gland,
 - Parathyroid gland, adrenal gland, pituitary gland, pancreas and gonads.
 - Metabolism of calcium
- 7. Nutrition**
- General principles of a balanced diet, effect of dietary deficiency, protein energy malnutrition, Kwashiorkor, marasmus.
 - Fluid and electrolytic balance in maintaining hemostasis and significance in minor and major surgical procedures.

Biochemistry: General principles governing the various biological activities of the body, such as osmotic pressure, electrolytes, dissociation, oxidation, reduction, etc. General composition of the body Intermediary metabolism; carbohydrates, proteins, lipids, and their metabolism; nucleoproteins, nucleic acid and nucleotides and their metabolism; enzymes, vitamins and minerals; Hormones Body and other fluids. Metabolism of inorganic elements; Detoxification in the body; Antimetabolites.

PATHOLOGY

- 1. Inflammation**
- Repair and regeneration, necrosis and gangrene
 - Role of component system in acute inflammation;
 - Role of arachidonic acid and its metabolites in acute inflammation;
 - Growth factors in acute inflammation
 - Role of molecular events in cell growth and intercellular signaling cell surface receptors
 - Role of NSAIDs in inflammation
 - Cellular changes in radiation injury and its manifestation.
- 2. Haemostasis**
- Role of endothelium in thrombogenesis.
 - Arterial and venous thrombi
 - Disseminated intravascular coagulation
- 3. Shock**
- Pathogenesis of hemorrhagic, neurogenic, septic, cardiogenic shock.
 - Circulatory disturbances, ischemia, hyperemia, venous congestion, edema, infarction.
- 4. Chromosomal abnormalities**
- Marfan's syndrome, Ehlers-Danlos syndrome, fragile X-syndrome.
- 5. Hypersensitivity**
- Anaphylaxis, type 2 hypersensitivity, type 3 hypersensitivity and cell mediated reaction and its clinical importance, systemic lupus erythematosus.
 - Infection and infective granulomas.
- 6. Neoplasia**
- Classification of tumors
 - Carcinogenesis and carcinogen—chemical, viral and microbial
 - Grading and staging of cancers, tumor angiogenesis, para-neoplastic syndrome, spread of tumors.
 - Characteristics of benign and malignant tumors.

7. Others

- Sex-linked agammaglobulinemia.
- AIDS
- Management of immun deficiency patients requiring surgical procedures
- DiGeorge syndrome
- Ghon's complex, post-primary pulmonary tuberculosis—pathology and pathogenesis.

8. Oral pathology

- Developmental disturbances of oral and paraoral structures
- Regressive changes of teeth
- Bacterial, viral and mycotic infections of oral cavity
- Dental caries,, diseases of pulp and periapical tissues
- Physical and chemical injuries of the oral cavity
- Oral manifestations of metabolic and endocrinal disturbances
- Diseases of jaw bones and TMJ
- Diseases of blood and blood forming organs in relation to oral cavity
- Cysts of the oral cavity
- Salivary gland diseases
- Role of laboratory investigations in oral surgery

9. Microbiology

- Immunity
- Knowledge of organisms commonly associated with disease of oral cavity.
- Morphology cultural characteristics of Strepto, Staphylo, Pneumo, gono, meningo, clostridium group of organism, spirochetes, organisms of TB, leprosy, diphtheria, actinomycosis and moniliasis.
- Hepatitis B and its prophylaxis
- Culture and sensitivity test
- Laboratory determinations
- Blood groups, blood matching, RBC and WBC count
- Bleeding and clotting time, etc., smears and cultures
- Urine analysis and cultures.

APPLIED PHARMACOLOGY AND THERAPEUTICS

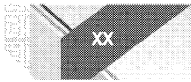
1. Definition of terminologies used
2. Dosage and mode of administration of drugs
3. Action and fate of drugs in the body
4. Drug addiction, tolerance and hypersensitivity reactions
5. Drugs acting on the CNS
6. General and local anesthetics, hypnotics, analeptics, and tranquilizers.
7. Chemotherapeutics and antibiotics
8. Analgesics and antipyretics
9. Antitubercular and antisiphilic drugs
10. Antiseptics, sialogogues and antisialogogues
11. Hematinics
12. Antidiabetics
13. Vitamins A, C, D, E, K and B-complex.

5. CONSERVATIVE DENTISTRY AND ENDODONTICS

COURSE CONTENTS

APPLIED ANATOMY OF HEAD AND NECK

- Development of face, paranasal sinuses and the associated structures and their anomalies, cranial and facial bones, TMJ anatomy and function, arterial and venous drainage of head and neck, muscles of face and neck including muscles of mastication and deglutition, brief consideration of structures and function of brain. Brief consideration of all cranial nerves and autonomic nervous system of head and neck. Salivary glands; Functional anatomy of mastication, deglutition and speech. Detailed anatomy of deciduous and permanent teeth, general consideration in physiology of permanent dentition, form, function, alignment, contact, occlusion.



- Internal anatomy of permanent teeth and its significance
- Applied histology—histology of skin, oral mucosa, connective tissue, bone cartilage, blood vessels, lymphatics, nerves, muscles, tongue.

DEVELOPMENT OF TEETH

- Enamel—development and composition, physical characteristics, chemical properties, structure.
- Age changes—clinical structure.
- Dentin—development, physical and chemical properties, structure type of dentin, innervations, age and functional changes.
- Pulp—development, histological structures, innervations, functions, regressive changes, clinical considerations.
- Cementum—composition, cementogenesis, structure, function, clinical consideration.
- Periodontal ligament—development, structure, function and clinical consideration.
- Salivary glands—structure, function, clinical considerations.
- Eruption of teeth.

APPLIED PHYSIOLOGY

- Mastication, deglutition, digestion and assimilation, fluid and electrolyte balance.
- Blood composition, volume, function, blood groups, hemostasis, coagulation, blood transfusion, circulation, heart, pulse, blood pressure, shock, respiration, control, anoxia, hypoxia, asphyxia, artificial respiration, and endocrinology—general principles of endocrine activity and disorders relating to pituitary, thyroid, parathyroid, adrenals including pregnancy and lactation.
- Physiology of saliva—composition, function, clinical significance.
- Clinical significance of vitamins, diet and nutrition—balanced diet.
- Physiology of pain, sympathetic and parasympathetic nervous system, pain pathways, physiology of pulpal pain; Odontogenic and non-odontogenic pain, pain disorders—typical and atypical, biochemistry such as osmotic pressure, electrolytic dissociation, oxidation, reduction, etc. Carbohydrates, proteins, lipids and their metabolism, nucleoproteins, nucleic acid and their metabolism. Enzymes, vitamins and minerals, metabolism of inorganic elements, detoxification in the body, antimetabolites, chemistry of blood lymph and urine.

PATHOLOGY

- Inflammation, repair, degeneration, necrosis and gangrene.
- Circulatory disturbances—ischemia, hyperemia, edema, thrombosis, embolism, infarction, allergy and hypersensitivity reaction.
- Neoplasms—classifications of tumors, characteristics of benign and malignant tumors, spread tumors.
- Blood dyscrasias
- Developmental disturbances of oral and paraoral structures, dental caries, regressive changes of teeth, pulp, periapical pathology, pulp reaction to dental caries and dental procedures.
- Bacterial, viral, mycotic infections of the oral cavity.

MICROBIOLOGY

- Pathways of pulpal infection, oral flora and micro-organisms associated with endodontic diseases, pathogenesis, host defense, bacterial virulence factors, healing, theory of focal infections, microbes or relevance to dentistry—strepto, staphylococci, lactobacilli, Corynebacterium, Actinomycetes, Clostridium, Neisseria, Vibrio, Bacterioids, fusobacteria, spirochetes, mycobacterium, virus and fungi.
- Cross infection, infection control, infection control procedure, sterilization and disinfection.
- Immunology—antigen-antibody reaction, allergy, hypersensitivity and anaphylaxis, autoimmunity, grafts, viral hepatitis, HIV infections and aids. Identification and isolation of microorganisms from infected root canals. Culture medium and culturing technique (Aerobic and anaerobic interpretation and antibiotic sensitivity test).

PHARMACOLOGY

- Dosage and route of administration of drugs, actions and fate of drug in body, drug addiction, tolerance of hypersensitivity reactions.
- Local anesthesia—agents and chemistry, pharmacological actions, fate and metabolism of anesthetic, ideal properties, techniques and complications.
- General anesthesia—pre-medications, neuromuscular blocking agents, induction agents, inhalation anesthesia, and agents used, assessment of anesthetic problems in medically compromised patients.
- Anesthetic emergencies
- Antihistamines, corticosteroids, chemotherapeutic and antibiotics, drug resistance, hemostasis, and hemostatic agents, anticoagulants, sympathomimetic drugs, vitamins and minerals (A, B, C, D, E, K, iron), antisialogogue, immunosuppressants, drug interactions, antiseptics, disinfectants, antiviral agents, drugs acting on CNS.

BIOSTATISTICS

- Introduction; Basic concepts; Sampling; Health information systems collection, compilation, presentation of data. Elementary statistical methods—presentation of statistical data; Statistical averages—measures of central tendency, measures of dispersion; Normal distribution. Tests of significance—parametric and non-parametric tests (Fisher exact test; Sign test; Median test; Mann Whitney test; Kruskal Wallis one way analysis, Friedman two way analysis, Regression analysis); Correlation and regression; Use of computers.

RESEARCH METHODOLOGY

- Essential features of a protocol for research in humans
- Experimental and non-experimental study designs
- Ethical considerations of research.

APPLIED DENTAL MATERIALS

- Physical and mechanical properties of dental materials, biocompatibility.
- Impression materials, detailed study of various restorative materials, restorative resin and recent advances in composite resins, bonding—recent developments—tarnish and corrosion, dental amalgam, direct filling gold, casting alloys, inlay wax, die materials, investments, casting procedures, defects, dental cements for restoration and pulp protection (luting, liners, bases) cavity varnishes.
- Dental ceramics—recent advances, finishing and polishing materials.
- Dental burs—design and mechanics of cutting—other modalities of tooth preparation.
- Methods of testing biocompatibility of materials used.

6. ORTHODONTICS AND DENTOFACIAL ORTHOPAEDICS

COURSE CONTENTS

I. APPLIED ANATOMY

- Prenatal growth of head: Stages of embryonic development, origin of head, origin of face, origin of teeth.
- Postnatal growth of head: Bones of skull, the oral cavity, development of chin, the hyoid bone, general growth of head, face growth.
- Bone growth: Origin of bone, composition of bone, units of bone structure, schedule of ossification, mechanical properties of bone, roentgen graphic appearance of bone.
- Assessment of growth and development: Growth prediction, growth spurts, the concept of normality and growth increments of growth, differential growth, gradient of growth, methods of gathering growth data. Theories of growth and recent advances, factors affecting physical growth.
- Muscles of mastication: Development of muscles, muscle change during growth, muscle function and facial development, muscle function and malocclusion.
- Development of dentition and occlusion: Dental development periods, order of tooth eruption, chronology of permanent tooth formation, periods of occlusal development, pattern of occlusion.
- Assessment of skeletal age: The carpal bones, carpal X-rays, cervical vertebrae.

II. PHYSIOLOGY

- **Endocrinology and its disorders**
(Growth hormone, thyroid hormone, parathyroid hormone, ACTH) pituitary gland hormones, thyroid gland hormones, parathyroid gland hormones
- **Calcium and its metabolism**
- **Nutrition—metabolism and their disorders:** Proteins, carbohydrates, fats, vitamins and minerals.
- **Muscle physiology**
- **Craniofacial biology:** Cell adhesion molecules and mechanism of adhesion
- **Bleeding disorders in orthodontics: Hemophilia**

III. DENTAL MATERIALS

- **Gypsum products:** dental plaster, dental stone and their properties, setting reaction, etc.
- **Impression materials:** impression materials in general and particularly of alginate impression material.
- **Acrylics:** chemistry, composition physical properties
- **Composites:** composition types, properties setting reaction
- **Banding and bonding cements:** Zn (PO₄), zinc silicophosphate, Zinc polycarboxylate, resin cements and glass Ionomer cements
- **Wrought metal alloys:** deformation, strain hardening, annealing, recovery, recrystallization, grain growth, properties of metal alloys
- **Orthodontic arch wires:** stainless steel gold, wrought cobalt chromium nickel alloys, alpha and beta titanium alloys
- **Elastics:** Latex and non-latex elastics.
- **Applied physics:** Bioengineering and metallurgy.
- **Specification and tests methods** used for materials used in Orthodontics
- **Survey of all contemporary literature and Recent advances** in above mentioned materials.

IV. GENETICS

- Cell structure, DNA, RNA, protein synthesis, cell division
- Chromosomal abnormalities
- Principles of orofacial genetics
- Genetics in malocclusion
- 5 Molecular basis of genetics
- Studies related to malocclusion
- Recent advances in genetics related to malocclusion
- Genetic counseling
- Bioethics and relationship to orthodontic management of patients.

V. PHYSICAL ANTHROPOLOGY

- Evolutionary development of dentition
- Evolutionary development of jaws.

VI. PATHOLOGY

- Inflammation
- Necrosis

VII. BIOSTATISTICS

- Statistical principles
 - o Data collection
 - o Method of presentation
 - o Method of summarizing
 - o Methods of analysis—different tests/errors
- Sampling and sampling technique
- Experimental models, design and interpretation
- Development of skills for preparing clear concise and cogent scientific abstracts and publication.

VIII. APPLIED RESEARCH METHODOLOGY IN ORTHODONTICS

- Experimental design
- Animal experimental protocol
- Principles in the development, execution and interpretation of methodologies in orthodontics.
- Critical Scientific appraisal of literature.

IX. APPLIED PHARMACOLOGY**X. ORTHODONTIC HISTORY**

- Historical perspective
- Evolution of orthodontic appliances
- Pencil sketch history of Orthodontic peers
- History of orthodontics in India.

XI. CONCEPTS OF OCCLUSION AND ESTHETICS

- Structure and function of all anatomic components of occlusion
- Mechanics of articulation
- Recording of masticatory function
- Diagnosis of occlusal dysfunction
- Relationship of TMJ anatomy and pathology and related neuromuscular physiology.

XII. ETIOLOGY AND CLASSIFICATION OF MALOCCLUSION

- A comprehensive review of the local and systemic factors in the causation of malocclusion.
- Various classifications of malocclusion.

XIII. DENTOFACIAL ANOMALIES

- Anatomical, physiological and pathological characteristics of major groups of developmental defects of the orofacial structures.

XIV. CHILD AND ADULT PSYCHOLOGY

- Stages of child development.
- Theories of psychological development.
- Management of child in orthodontic treatment.
- Management of handicapped child.
- Motivation and psychological problems related to malocclusion/orthodontics.
- Adolescent psychology.
- Behavioral psychology and communication.

7. ORAL PATHOLOGY AND ORAL MICROBIOLOGY**COURSE CONTENTS****1. BIOSTATISTICS AND RESEARCH METHODOLOGY**

- Basic principles of biostatistics and study as applied to dentistry and research.
- Collection/organization of data/measurement scales presentation of data and analysis.
- Measures of central tendency.
- Measures of variability.
- Sampling and planning of health survey.
- Probability, normal distribution and indicative statistics.
- Estimating population values.
- Tests of significance (parametric/non-parametric qualitative methods).
- Analysis of variance
- Association, correlation and regression.

2. APPLIED GROSS ANATOMY OF HEAD AND NECK INCLUDING HISTOLOGY

- Temporomandibular joint
- Trigeminal nerve and facial nerve
- Muscles of mastication
- Tongue
- Salivary glands
- Nerve supply; blood supply, lymphatic drainage and venous drainage of orofacial tissues.
- Embryology
 - Development of face, palate, mandible, maxilla, tongue and applied aspects of the same

- Development of teeth and dental tissues and developmental defects of oral and maxillofacial region and abnormalities of teeth
- Maxillary sinus
- Jaw muscles and facial muscles.

Genetics: Introduction modes of inheritance, chromosomal anomalies of oral tissues and single gene disorders.

3. PHYSIOLOGY (GENERAL AND ORAL)

- Saliva
- Pain
- Mastication
- Taste
- Deglutition
- Wound healing
- Vitamins. (influence on growth, development and structure of oral soft and hard tissues and paraoral tissues.)
- Calcium metabolism.
- Theories of mineralization
- Tooth eruption and shedding
- Hormones. (Influence on growth, development and structure of oral soft and hard tissues and para oral tissues.)
- Blood and its constituents.

4. CELL BIOLOGY

- Cell-structure and function (ultrastructural and molecular aspects), intercellular junctions, cell cycle and division, cell cycle regulators, cell to cell and cell—extracellular matrix interactions.
- Detailed molecular aspects of DNA, RNA, and intracellular organelles, transcription and translation and molecular biology techniques.

5. GENERAL HISTOLOGY

Light and electron microscopy considerations of epithelial tissues and glands, bone, hematopoietic system, lymphatic system, muscle, neural tissue, endocrinal system (thyroid, pituitary, parathyroid).

6. BIOCHEMISTRY

- Chemistry of carbohydrates, lipids and proteins.
- Methods of identification and purification.
- Metabolism of carbohydrates, lipids and proteins.
- Biological oxidation.
- Various techniques—cell fractionation and ultrafiltration, centrifugation, electrophoresis, spectrophotometry, and radioactive techniques.

7. GENERAL PATHOLOGY

Inflammation and chemical mediators, thrombosis, embolism, necrosis, repair, degeneration, shock, hemorrhage pathogenic mechanisms at molecular level and blood dyscrasias; Carcinogenesis and neoplasia.

8. GENERAL MICROBIOLOGY

- Definitions of various types of infections
- Routes of infection and spread
- Sterilization, disinfection and antiseptics
- Bacterial genetics
- Physiology and growth of microorganisms

9. BASIC IMMUNOLOGY

- Basic principles of immunity, antigen and antibody reactions.
- Cell mediated immunity and Humoral immunity.
- Immunology of hypersensitivity.
- Immunological basis of the autoimmune phenomena.
- Immunodeficiency with relevance to opportunistic infections.
- Basic principles of transplantation and tumor immunity.

10. SYSTEMIC MICROBIOLOGY/APPLIED MICROBIOLOGY

Morphology, classification, pathogenicity, mode of transmission, methods of prevention, collection and transport of specimen, for

laboratory diagnosis, staining methods, common culture media, interpretation of laboratory reports and antibiotic sensitivity tests.

- Staphylococci
- Streptococci
- *Corynebacterium diphtheria*
- Mycobacteria
- Clostridia, Bacteroides and fusobacteriae
- Actinomycetales
- Spirochetes

Virology

General properties: Structure, broad classification of viruses, pathogenesis, pathology of viral infections.

Herpesvirus: List of viruses included, lesions produced, pathogenesis, latency principles and laboratory diagnosis.

Hepatitis virus: List of viruses, pathogenesis, and mode of infection, list of diagnostic tests, and their interpretations, methods of prevention and control.

Human immunodeficiency virus: Structure with relevance to laboratory diagnosis, type of infection, laboratory tests and their interpretation, universal precautions, specific precautions and recent trends in diagnosis and prophylaxis.

Mycology

- General properties of fungi, classification bases on disease, superficial, subcutaneous, deep opportunistic infections.
- General principles of fungal infections, diagnosis rapid diagnosis method of collection of sample and examination for fungi.

11. ORAL BIOLOGY (ORAL AND DENTAL HISTOLOGY)

- Structure and function of oral, dental and paraoral tissues including their ultrastructure, molecular and biochemical aspects.
- Study of morphology of permanent and deciduous teeth.

8. PUBLIC HEALTH DENTISTRY

COURSE CONTENTS

Applied Basic Sciences

I. APPLIED ANATOMY AND HISTOLOGY

A. Applied Anatomy in relation to

- Development of face
- Branchial arches
 - Muscles of facial expression
 - Muscles of mastication
 - TMJ
 - Salivary gland
 - Tongue
 - Hard and soft palate
 - Infratemporal fossa
 - Paranasal air sinuses
 - Pharynx and larynx
 - Cranial and spinal nerves- with emphasis on trigeminal, facial, glossopharyngeal and hypoglossal nerve
- Osteology of maxilla and mandible
 - Blood supply, venous and lymphatic drainage of head and neck
 - Lymph nodes of head and neck
 - Structure and relations of alveolar process and edentulous mouth
 - Genetics—fundamentals

B. Oral Histology

- Development of dentition, Innervations of dentin and pulp
- Periodontium-development, histology, blood supply, nerve supply and lymphatic drainage
- Oral mucous membrane
- Pulp-periodontal complex

II. APPLIED PHYSIOLOGY AND BIOCHEMISTRY

- Cell
- Mastication and deglutition
- Food and nutrition
- Metabolism of carbohydrates, proteins and fats
- Vitamins and minerals
- Fluid and electrolyte balance
- Pain pathway and mechanism—types, properties
- Blood composition and functions, clotting mechanism and erythropoiesis, Blood groups and transfusions, Pulse and blood pressure
- Dynamics of blood flow
- Cardiovascular homeostasis—heart sounds
- Respiratory system: Normal physiology and variations in health and diseases; asphyxia and artificial respiration
- Endocrinology: Thyroid, parathyroid, adrenals, pituitary, sex hormones and pregnancy, Endocrine regulation of blood sugar.

III. A. APPLIED PATHOLOGY

- Pathogenic mechanism of molecular level
- Cellular changes following injury
- Inflammation and chemical mediators
- Edema, thrombosis and embolism
- Hemorrhage and shock
- Neoplasia and metastasis
- Blood disorders
- Histopathology and pathogenesis of dental caries, periodontal disease, oral mucosal lesions, and malignancies, HIV
- Propagation of dental infection

B. MICROBIOLOGY

- Microbial flora of oral cavity
- Bacteriology of dental caries and periodontal disease
- Methods of sterilization
- Virology of HIV, herpes, hepatitis
- Parasitology
- Basic immunology—basic concepts of immune system in human body
 - Cellular and humoral immunity
 - Antigen and antibody system
 - Hypersensitivity
 - Autoimmune diseases

C. ORAL PATHOLOGY

- Detailed description of diseases affecting the oral mucosa, teeth, supporting tissues and jaws.

IV. PHYSICAL AND SOCIAL ANTHROPOLOGY

- Introduction and definition
- Appreciation of the biological basis of health and disease
- Evolution of human race, various studies of different races by anthropological methods.

V. APPLIED PHARMACOLOGY

- Definition, scope and relations to other branches of medicine, mode of action, bioassay, standardization, pharmacodynamics, pharmacokinetics.
- Chemotherapy of bacterial infections and viral infections – sulphonamides and antibiotics.
- Local anesthesia
- Analgesics and anti-inflammatory drugs
- Hypnotics, tranquilizers and antipyretics
- Important hormones—ACTH, cortisone, insulin and oral antidiabetics.
- Drug addiction and tolerance
- Important pharmacological agents in connection with autonomic nervous system—adrenaline, noradrenaline, atropine

- Brief mention of antihypertensive drugs
- Emergency drugs in dental practice
- Vitamins and haemopoietic drugs.

VI. RESEARCH METHODOLOGY AND BIOSTATISTICS

Health informatics—basic understanding of computers and its components, operating software (Windows), Microsoft office, preparation of teaching materials like slides, project, multimedia knowledge.

Research methodology—definitions, types of research, designing written protocol for research, objectivity in methodology, quantification, records and analysis.

Biostatistics—introduction, applications, uses and limitations of bio – statistics in Public Health dentistry, collection of data, presentation of data, measures of central tendency, measures of dispersion, methods of summarizing, parametric and non parametric tests of significance, correlation and regression, multivariate analysis, sampling and sampling techniques—types, errors, bias, trial and calibration.

Computers: Basic operative skills in analysis of data and knowledge of multimedia.

9. PAEDODONTICS AND PREVENTIVE DENTISTRY

COURSE CONTENTS

1. Applied Anatomy and genetics
2. Applied Physiology
3. Applied Pathology
4. Nutrition and Dietics
 - Growth and Development: Prenatal and postnatal development of cranium, face, jaws, teeth and supporting structures. Chronology of dental development and development of occlusion. Dimensional changes in dental arches. Cephalometric evaluation of growth.
 - Child Psychology: Development and classification of behavior, personality, intelligence in children, theories of child psychology, stages of psychological child development, fear anxiety, apprehension and its management.
 - Behavior Management: Non-pharmacological and pharmacological methods.
 - Child Abuse and dental neglect
 - Conscious Sedation, Deep Sedation and General Anesthesia in Pediatric Dentistry: (Including other drugs, synergic and antagonistic actions of various drugs used in children.
 - Preventive Pedodontics: Concepts, chair side preventive measures for dental diseases, high-risk caries including rampant and extensive caries: Recognition; Features and Preventive Management; Pit and fissures sealants; Oral hygiene measures, Correlation of brushing with dental caries and periodontal diseases. Diet and nutrition as related to dental caries. Diet Counseling.
 - Dental Plaque: Definition; Initiation; Pathogenesis; Biochemistry; Morphology; and Metabolism.
 - Microbiology and Immunology as Related to Oral Diseases in Children: Basic concepts, immune system in human body; Auto-immune diseases; Histopathology; Pathogenesis; Immunology of dental caries; Periodontal diseases; Tumors, Oral mucosal lesions, etc.
 - Gingival and Periodontal Diseases in Children:
 - Normal gingiva and periodontium in children.
 - Gingival and periodontal diseases: Etiology; Pathogenesis; Prevention and Management.
 - Pediatric Operative Dentistry
 - Principle of operative dentistry along with modifications of materials/past, current and latest including tooth-colored materials.
 - Modifications required for cavity preparation in primary and young permanent teeth.
 - Various isolation techniques

- Restorations of decayed primary, young permanent and permanent teeth in children using various restorative material like Glass ionomer; Composites; Silver; Amalgam and latest material (gallium).
 - Stainless steel; Polycarbonate and resin crowns/Veneers and fibre pit systems.
11. Pediatric Endodontics:
 - a. Primary dentition: Diagnosis of pulpal diseases and their management: Pulp capping; Pulpotomy; Pulpectomy (Materials and Methods); Controversies and recent concepts.
 - b. Young permanent teeth and permanent teeth, Pulp capping, Pulpotomy; Apexogenesis; Apexification, Concepts, Techniques and Materials used for different procedures.
 - c. Recent advances in pediatric diagnosis and endodontics.
 12. Prosthetic Consideration in Paediatric Dentistry.
 13. Traumatic Injuries in Children:
 - Classifications and importance.
 - Sequelae and reaction of teeth to trauma.
 - Management of traumatized teeth with latest concepts.
 - Management of jaw fracture in children.
 14. Interceptive Orthodontics:
 - a. Concepts of occlusion and hesthetics: Structure and function of all anatomic components of occlusion, mechanics of articulations, recording of masticatory function, diagnosis of Occlusal dysfunction, relationship of TMJ anatomy and pathology and related neuromuscular physiology.
 - b. A comprehensive review of the local and systemic factors in the causation of malocclusion.
 - c. Recognition and management of normal and abnormal developmental occlusions in primary, mixed and permanent dentitions in children (occlusal guidance).
 - d. Biology of tooth movement: A comprehensive review of the principles of teeth movement.
Review of contemporary literature. Histopathology of bone and periodontal ligament; Molecular and ultracellular consideration in tooth movement.
 - e. Myofunctional appliances: Basic principles, contemporary appliances: Design and fabrication.
 - f. Removable appliances: Basic principles, contemporary appliances: Design and fabrication
 - g. Case selection and diagnosis in interceptive orthodontics (cephalometrics; Image processing; Tracing; Radiation hygiene; Videomaging and advance; Cephalometric techniques).
 - h. Space Management: Etiology; Diagnosis of space problems, analysis; Biomechanics; Planned extraction in interception orthodontics.
 15. Oral Habits in Children:
 - Definition; Etiology and Classification
 - Clinical features of digit sucking, tongue thrusting, mouth breathing and various other secondary habits.
 - Management of oral habits in children
 16. Dental Care of Children with Special Needs:
 - Definition Etiology; Classification; Behavioral; Clinical features and Management of children with:
 - Physically handicapping conditions
 - Mentally compromising conditions
 - Medically compromising conditions
 - Genetic disorders
 17. Oral manifestations of Systemic Conditions in Children and their Management
 18. Management of Minor Oral Surgical Procedures in Children
 19. Dental Radiology as Related to Pediatric Dentistry
 20. Cariology
 - Historical background
 - Definition; aetiology and pathogenesis
 - Caries pattern in primary, young permanent and permanent teeth in children.
 - Rampant caries, early childhood caries and extensive caries. Definition; Etiology; Pathogenesis; Clinical features; Complications and Management.
 - Role of diet and nutrition in dental caries
 - Dietary modifications and diet counseling.
 - Subjective and objective methods of caries detection with emphasis on Caries activity tests; Caries prediction; Caries susceptibility and their clinical applications.
 21. Pediatric Oral Medicine and Clinical Pathology: Recognition and management of developmental dental anomalies, teething disorders, stomatological conditions, mucosal lesions, viral infections, etc.
 22. Congenital Abnormalities in Children: Definition; Classification; Clinical features and Management.
 23. Dental Emergencies in Children and their Management.
 24. Dental Materials used in Pediatric Dentistry.
 25. Preventive Dentistry:
 - Definition
 - Principles and scope
 - Types of prevention
 - Different preventive measures used in pediatric dentistry including fissure sealants and caries vaccine.
 26. Dental Health Education and School Dental Health Programmes.
 27. Dental health concepts; Effects of civilization and environment; Dental Health delivery system; Public Health measures related to children along with principles of Pediatric Preventive Dentistry.
 28. Fluorides:
 - Historical background
 - Systemic and topical fluorides
 - Mechanism of action
 - Toxicity and management.
 - Defluoridation techniques.
 29. Medicological Aspects in Paediatric Dentistry with Emphasis on Informed Concept.
 30. Counseling in Paediatric Dentistry
 31. Case History Recording, Outline of Principles of Examination, Diagnosis and Treatment Planning.
 32. Epidemiology: Concepts, methods of recording and evaluation of various oral diseases. Various national and global trends of epidemiology of oral diseases.
 33. Comprehensive Infant Oral Health Care.
 34. Principles of Biostatistics and Research Methodology and Understanding of computers and Photography.
 35. Comprehensive Cleft Care Management with Emphasis on Counseling, Feeding, Nasoalveolar Bone Remodeling, Speech Rehabilitation.
 36. Setting up of Pedodontics and Preventive Dentistry Clinic.
 37. Emerging Concept in Paediatric Dentistry of Scope of Laser/ Minimum Invasive Procedures: Pediatric Dentistry.

10. ORAL MEDICINE AND RADIOLOGY

COURSE CONTENTS

I. Applied Anatomy

1. Gross anatomy of the face
 - a. Muscles of facial expression and muscles of mastication
 - b. Facial nerve
 - c. Facial artery
 - d. Facial vein
 - e. Parotid gland and its relations
2. Neck region
 - a. Triangles of the neck with special reference to carotid; Digastric triangles and midline structures
 - b. Facial spaces

- c. Carotid system of arteries; vertebral artery, and subclavian arteries.
 - d. Jugular system
 - Internal jugular
 - External jugular
 - e. Lymphatic drainage
 - f. Cervical plane
 - g. Muscles derived from pharyngeal arches
 - h. Infratemporal fossa in detail and temporomandibular joint
 - i. Endocrine glands pituitary,
 - Thyroid
 - Parathyroid
 - j. Sympathetic chain
 - k. Cranial nerves—V, VII, IX, XI, and XII
 - l. Exocrine glands
 - Parotid
 - Thyroid
 - Parathyroid
3. Oral cavity
- a. Vestibule and oral cavity proper
 - b. Tongue and teeth
 - c. Palate—soft and hard
4. Nasal cavity
- a. Nasal septum
 - b. Lateral wall of nasal cavity
 - c. Paranasal air sinuses
5. Pharynx: Gross salient features of brain and spinal cord with references to attachment of cranial nerves to the brainstem.
Detailed study of the cranial nerve nuclei of V, VII, IX, X, XI, XII
Osteology: Comparative study of fetal and adult skull.
Mandible: Development, ossification, age changes and evaluation of mandible in detail.

II. EMBRYOLOGY

1. Development of face, palate, nasal septum and nasal cavity, paranasal air sinuses
2. Pharyngeal apparatus in detail including the floor of the primitive pharynx
3. Development of tooth in detail and the age changes
4. Development of salivary glands
5. Congenital anomalies of face must be dealt in detail.

III. HISTOLOGY

1. Study of epithelium of oral cavity and the respiratory tract
2. Connective tissue
3. Muscular tissue
4. Nervous tissue
5. Blood vessels
6. Cartilage
7. Bone and tooth
8. Tongue
9. Salivary glands
10. Tonsil, thymus, lymph nodes

IV. PHYSIOLOGY

1. General physiology:
 - Cell
 - Body fluid compartments
- Classification; Composition**
- Cellular transport
 - RMP and action potential

V. MUSCLE NERVE PHYSIOLOGY

1. Structure of a neuron and properties of nerve fibers
2. Structure of muscle fibers and properties of muscle fibers
3. Neuromuscular transmission
4. Mechanism of muscle contraction

VI. BLOOD

1. RBC and Hb
2. WBC—Structure and functions
3. Platelets—functions and applied aspects
4. Plasma proteins
5. Blood coagulation with applied aspects
6. Blood groups
7. Lymph and applied aspects

VII. RESPIRATORY SYSTEM

- Air passages, composition of air, dead space, mechanics of respiration with pressure and volume changes
- Lung volumes and capacities and applied aspects
- Oxygen and carbon dioxide transport
- Neural regulation of respiration
- Chemical regulation of respiration
- Hypoxia, effects of increased barometric pressure and decreased barometric pressure.

VIII. CARDIOVASCULAR SYSTEM

- Cardiac cycle
- Regulation of heart rate/ stroke volume/ cardiac output/ blood flow
- Regulation of blood pressure
- Shock, hypertension, cardiac failure.

IX. EXCRETORY SYSTEM

- Renal function tests.

Gastrointestinal Tract

Composition, functions and regulation of:

- Saliva
- Gastric juice
- Pancreatic juice
- Bile and intestinal juice
- Mastication and deglutition

X. ENDOCRINE SYSTEM

- Hormones—classification and mechanism of action
- Hypothalamic and pituitary hormones
- Thyroid hormones
- Parathyroid hormones and calcium homeostasis
- Pancreatic hormones
- Adrenal hormones

XI. CENTRAL NERVOUS SYSTEM

- Ascending tract with special references to pain pathway

XII. SPECIAL SENSES

- Gustation and Olfaction

XIII. BIOCHEMISTRY

1. **Carbohydrates:** Disaccharides specifically maltose, lactose, sucrose
 - Digestion of starch/absorption of glucose
 - Metabolism of glucose, specifically glycolysis, TCA cycle, gluconeogenesis
 - Blood sugar regulation
 - Glycogen storage regulation
 - Glycogen storage diseases
 - Galactosemia and fructosemia
2. **Lipids**
 - Fatty acids: Essential/non essential
 - Metabolism of fatty acids—oxidation, ketone body formation, utilization ketosis
 - Outline of cholesterol metabolism—synthesis and products formed from cholesterol

3. Protein

- Amino acids—essential/non essential, complete/incomplete proteins
- Transamination/Deamination (definition with examples)
- Urea cycle
- Tyrosine: Hormones synthesized from tyrosine
- Inborn errors of amino acid metabolism
- Methionine and transmethylation

4. Nucleic Acids

- Purines/Pyrimidines
- Purine analogs in medicine
- DNA/RNA: Outline of structure
- Transcription/translation
- Steps of protein synthesis
- Inhibitors of protein synthesis
- Regulation of gene function

5. Minerals

- Calcium/Phosphorus metabolism specifically regulation of serum calcium levels
- Iron metabolism
- Iodine metabolism
- Trace elements in nutrition

6. Energy Metabolism

- Basal metabolic rate
- Specific dynamic action (SDA) of foods

7. Vitamins

Mainly these vitamins and their metabolic role—specifically vitamin A, vitamin C, vitamin D, thiamin, riboflavin, niacin, pyridoxine.

XIV. PATHOLOGY**1. Inflammation:**

- Repair and regeneration, necrosis and gangrene
- Role of complement system in acute inflammation
- Role of arachidonic acid and its metabolites in acute inflammation
- Growth factors in acute inflammation
- Role of molecular events in cell growth and intercellular signaling cell surface receptors
- Role of NSAIDS in inflammation
- Cellular changes in radiation injury and its manifestations

Homeostasis:

- Role of Endothelium in thrombogenesis
- Arterial and venous thrombi
- Disseminated intravascular coagulation

Shock

- Pathogenesis of hemorrhagic, neurogenic, septic, cardiogenic shock, circulatory disturbances, ischemic hyperemia, venous congestion, edema, infarction; Chromosomal abnormalities:
- Marfan's syndrome
- Ehlers-Danlos syndrome
- Fragile X syndrome

Hypersensitivity

- Anaphylaxis
- Type II Hypersensitivity
- Type III Hypersensitivity
- Cell mediated reaction and its clinical importance
- Systemic lupus erythematosus
- Infection and infective granulomas

Neoplasia

- Classification of tumors
- Carcinogenesis and Carcinogens: Chemical, viral and microbial
- Grading and staging of cancer, tumor angiogenesis, paraneoplastic syndrome.

- Spread of tumors
- Characteristics of benign and malignant tumors

Others:

- Sex linked agammaglobulinemia
- AIDS

Management of Immune deficiency patients requiring surgical procedures

- DiGeorge syndrome
- Ghon's complex.

XV. PHARMACOLOGY

1. Definition of terminologies used
2. Dosage and mode of administration of drugs
3. Action and fate of drugs in the body
4. Drugs acting on the CNS
5. Drug addiction, tolerance and hypersensitive reactions
6. General and local anesthetics, hypnotics, antiepileptics, and tranquilizers
7. Chemotherapeutics and antibiotics
8. Analgesics and antipyretics
9. Antitubercular and antisyphilitic drugs
10. Antiseptics, sialogogues, and antisialogogues
11. Hematinics.
12. Antidiabetics
13. Vitamins A, C, D, E, K and B-complex
14. Steroids

11. ETHICS IN DENTISTRY**COURSE CONTENTS****Introduction to ethics**

- What are ethics?
- What are values and norms?
- How to form a value system in one's personal and professional life?
- Hippocratic oath.
- Declaration of Helsinki, WHO declaration of Geneva, International code of ethics, D.C.I. Code of ethics.

Ethics of the individual

- The patient as a person. Right to be respected Truth and confidentiality Autonomy of decision
- Doctor Patient relationship

Professional Ethics

- Code of conduct
- Contract and confidentiality charging of fees, fee splitting prescription of drugs
- Over-investigating the patient
- Malpractice and negligence

Research ethics

- Animal and experimental research/humanness
- Human experimentation
- Human volunteer research—inform consent
- Drug trials
- Ethical workshop of cases gathering all scientific factors; Gathering all value factors
- Identifying areas of value—conflict, setting of priorities
- Working out criteria towards decisions.

LIST OF INDIAN UNIVERSITIES INCLUDED (1990–2015)

1. Tamil Nadu M.G.R. Medical University (TNMGR).
2. Kerala University of Health Science (KUHS).
3. Rajiv Gandhi University of Health Sciences (RGUHS).
4. Manipal Academy of Higher Education (MAHE).
5. Maharashtra University of Health Science (MUHS).
6. Himachal Pradesh University (HP University).
7. Baba Farid University of Health Science (BFUHS).
8. University of Health Sciences, Rohtak (UHSR)
9. Rajasthan University of Health Sciences (RUHS)
10. Sumandeep Vidyapeeth University.
11. Pacific University.
12. Bangalore University.
13. Nagpur University.
14. Gujarat University.
15. Bombay University.

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Anatomy, Embryology and Histology

1. OSTEOLOGY

Q. 1. Discuss the development of mandible in detail. Write about age changes in mandible.

(BFUHS, Nov. 2007; TNMGR, Sept. 2010; RUHS, May 2015)

Ans.

A. Development of mandible: Most of the bone is formed in membrane in the mesenchyme of the mandibular process. The ventral part of Meckel's cartilage gets embedded in the bone. The condylar and coronoid processes are ossified from secondary cartilage that appears in these situations.

B. Age changes

1. *In infants and children*

- The two halves of the mandible fuse during the first year of life.
- At birth, the mental foramen opens below the sockets for the two deciduous molar teeth near the lower border. The mandibular canal runs near the lower border. The foramen and canal gradually shift upwards.
- The angle is obtuse. It is 140° or more because the head is in-line with the body. The coronoid process is large and projects upwards above the level of condyle.

2. *In adults*

- The mental foramen opens midway between the upper and lower borders. The mandibular canal runs parallel with mylohyoid line.
- The angle reduces to about 110° or 120° because the ramus becomes almost vertical.

3. *In old age*

- Teeth fall out and the alveolar border is absorbed, so that the height of body is markedly reduced.

- The mental foramen and the mandibular canal are close to the alveolar border.

- The angle again becomes obtuse about 140° because the ramus is oblique.

Q. 2. Discuss in detail about the maxilla. Write about age changes in maxilla. (BFUHS, Nov. 2007)

Ans. Each maxilla has a body and four processes, the frontal, zygomatic, alveolar and palatine. The body of maxilla is pyramidal in shape, with its base directed medially at the nasal surface, and the apex directed laterally at the zygomatic process. It has four surfaces and encloses a large cavity, the maxillary sinus. The surfaces are given below.

I. Anterior or Facial Surface

- Anterior surface is directed forwards and laterally.
- Above the incisor teeth, there is a slight depression, the incisive fossa, which gives origin to depressor septi. Incisivus arises from the alveolar margin below the fossa and the nasalis superolateral to the fossa along the nasal notch.
- Lateral to canine eminence, there is a larger and deeper depression, the canine fossa, which gives origin to levator anguli oris.
- Above the canine fossa, there is infraorbital foramen, which transmits infraorbital nerve and vessels.
- Levator labii superioris arises between the infra-orbital margin and infraorbital foramen.
- Medially, the anterior surface ends in a deeply concave border, the nasal notch, which terminates below into process with the corresponding process of opposite maxilla forms the anterior nasal spine. Anterior surface bordering the nasal notch gives origin to nasalis and depressor septi.

II. Posterior or Infratemporal Surface

1. Posterior surface is convex and directed backwards and laterally.
2. It forms the anterior wall of infratemporal fossa, and is separated from anterior surface by the zygomatic process and a rounded ridge which descends from the process to the first molar tooth.
3. Near the centre of the surface open two or three alveolar canals for posterior superior alveolar nerve and vessels.
4. Posteroinferiorly, there is a rounded eminence, the maxillary tuberosity, which articulates superomedially with pyramidal process of palatine bone, and gives origin laterally to the superficial head of medial pterygoid muscle.
5. Above the maxillary tuberosity, the smooth surface forms anterior wall of pterygopalatine fossa, and is grooved by maxillary nerve.

III. Superior or Orbital Surface

1. Superior surface is smooth, triangular and slightly concave, and forms the greater part of the floor of orbit.
2. Anterior border forms a part of infraorbital margin. Medially, it is continuous with the lacrimal crest of the frontal process.
3. Posterior border is smooth and rounded; it forms most of the anterior margin of inferior orbital fissure. In the middle, it is notched by the infraorbital groove.
4. Medial border presents anteriorly the lacrimal notch which is converted into nasolacrimal canal by the descending process of lacrimal bone. Behind the notch, the border articulates from before backwards with the lacrimal, labyrinth of ethmoid, and the orbital process of palatine bone.
5. The surface presents infraorbital groove leading forwards to infraorbital canal which opens on the anterior surface as infraorbital foramen. The groove, canal and foramen transmit the infraorbital nerve and vessels. Near the midpoint, the canal gives off laterally a branch, the canalis sinuous, for the passage of anterior superior alveolar nerve and vessels.
6. Inferior oblique muscle of eyeball arises from a depression just lateral to lacrimal notch at the anteromedial angle of the surface.

IV. Medial or Nasal Surface

1. Medial surface forms a part of the lateral wall of nose.

2. Posterosuperiorly, it displays a large irregular opening of the maxillary sinus, the maxillary hiatus.
3. Above the hiatus, there are parts of air sinuses which are completed by the ethmoid and lacrimal bones.
4. Below the hiatus, the smooth concave surface forms a part of inferior meatus of nose.
5. Behind the hiatus, the surface articulates with perpendicular plate of palatine bone, enclosing the greater palatine canal which runs downwards and forwards, and transmits greater palatine vessels and the anterior, middle and posterior palatine nerves.
6. In front of the hiatus, there is nasolacrimal groove, which is converted into the nasolacrimal canal by articulation with the descending process of lacrimal bone and the lacrimal process of inferior nasal concha. The canal transmits nasolacrimal duct to the inferior meatus of nose.
7. More anteriorly, an oblique ridge forms the conchal crest for articulation with the inferior nasal concha.
8. Above the conchal crest, the shallow depression forms a part of the atrium of middle meatus of nose.

Age Changes

1. At birth

- a. The transverse and anteroposterior diameters are more than the vertical diameter.
- b. Frontal process is well marked.
- c. Body consists of a little more than the alveolar process, the tooth sockets reaching to the floor of orbit.
- d. Maxillary sinus is a mere furrow on the lateral wall of nose.

2. **In the adults:** Vertical diameter is greatest due to development of the alveolar process and increase in the size of the sinus.

3. **In the old:** The bone reverts to infantile condition. Its height is reduced as a result of absorption of the alveolar process.

Q. 3. Write a short note on hyoid bone.

(TNMGR, Sept. 2009; KUHS, Jan. 2014)

Ans. The hyoid bone is U-shaped. It develops from second and third branchial arches. It is situated in the anterior midline of the neck between the chin and the thyroid cartilage. At rest, it lies at the level of the third cervical vertebra behind and the base of the mandible in front. It is kept suspended in position by muscles and ligament. The hyoid bone provides attachment to

the floor of the mouth and to the tongue above, to the larynx below, and to the epiglottis and pharynx behind. The bone consists of the central part, called the body, and of two pairs of cornua, greater and lesser.

Body: It has anterior and posterior surfaces, and upper and lower borders. The anterior surface is convex and is directed forwards and upwards. It is often divided by a median ridge into two lateral halves. The posterior surface is concave and is directed backwards and downwards. Each lateral end of the body is continuous posteriorly with the greater horn or cornua.

Greater cornua: These are flattened from above downwards. Each cornua tapers posteriorly, but ends in a tubercle. It has two surfaces—upper and lower, two borders—medial and lateral and a tubercle.

Lesser cornua: These are small conical pieces of bone which project upwards from the junction of the body and greater cornua. The lesser cornua are connected to the body by fibrous tissue. Occasionally, they are connected to the greater cornua by synovial joints which usually persist throughout life, but may get ankylosed.

Attachments on Hyoid Bone

1. **Anterior surface of the body:** Insertion to geniohyoid and mylohyoid muscles, origin to hyoglossus.
2. **Upper border of the body:** Insertion to the lower fibers of the genioglossi and attachment to the thyrohyoid membrane.
3. **Lower border of the body:** Attachment to the pretracheal fascia. In front of the fascia, the sternohyoid is inserted medially and the omohyoid laterally. Below the omohyoid, there is the linear attachment of the thyrohyoid, extending back to the lower border of the greater cornua.
4. **Medial border of the greater cornua:** Attachment to the thyrohyoid membrane, stylohyoid muscle and digastric pulley.
5. **Lateral border of the greater cornua:** Insertion to the thyrohyoid muscle anteriorly. The investing fascia is attached throughout its length.
6. **Lesser cornua:** Provide attachment to the stylohyoid ligament at its tip. The middle constrictor muscle arises from its posterolateral aspect extending onto the greater cornua.

2. FACE, SCALP AND TEMPLE

Q. 1. Write a note on scalp. (Gujarat Uni., Oct. 2004)

Ans. The scalp is made of 5 layers.

1. **Skin** is thick and hairy, adherent to the epicranial aponeurosis through the dense superficial fascia.

2. **Subcutaneous or superficial fascia** is more fibrous and dense in the centre than at the periphery of the head. It binds the skin to the subjacent aponeurosis and provides proper medium for passage of vessels and nerves to the skin.
3. **Epicranial aponeurosis or galea aponeurotica** is freely movable on the pericranium along with the overlying and adherent skin and fascia.
4. **Loose areolar tissue** extends anteriorly into the eyelids because the frontalis muscles have no bony attachment; posteriorly to the highest and superior nuchal line and on each side to the superior temporal lines.
5. **Pericranium** is loosely attached to the surface of the bones, but is firmly adherent to their suture where the sutural ligaments bind the pericranium to the endocranium.

Arterial Supply

- a. **In front of auricle:** Supratrochlear, supraorbital, superficial temporal arteries.
- b. **Behind the auricle:** Posterior auricle, occipital arteries.

Venous Supply

- a. Supratrochlear and supraorbital vein combines to form angular vein, which continues as facial vein.
- b. Superficial temporal vein.
- c. Emissary veins.

Lymphatic

Parotid and mastoid lymph nodes.

Nerve Supply

Branches of trigeminal, auricle and facial nerves.

Q. 2. Write a note on danger area of face.

(RGUHS, May 2007)

Ans. Danger area of face comprises upper lip, lower part of nose and adjacent area. This area has been so named because boils, infections of the nose and injuries around the nose, especially those that become infected can readily spread to cavernous sinus resulting in cavernous sinus thrombosis (CST). CST is generally a fulminate process with high rates of morbidity and mortality.

Anatomical considerations: Anterior facial vein begins at the side of root of nose through the union of supraorbital and frontal veins. The vein drains upper lip, septum of nose and adjacent areas. The anterior facial vein communicates with the cavernous sinus through the ophthalmic veins. It also communicates with cavernous sinus via deep facial vein which connects the pterygoid plexus with anterior facial vein.

Anterior facial vein has no valves and it makes possible bidirectional blood flow in the vein. Dangerous area of face is lacking in deep fascia, which acts as barrier to the spread of inflammation and the infective processes. The highly anastomotic and valve less venous system allows retrograde spread of infection to the cavernous sinus via the superior and inferior ophthalmic veins.

Q. 3. Write a note on muscles of facial expression.

(RGUHS, 2006; TNMGR, Sept. 2008; BFUHS, May 2011; UHSR, April 2009)

Ans. The facial muscles or the muscles of facial expression are the subcutaneous muscles. They bring about different facial expressions. *Embryologically*, they develop from the mesoderm of the second branchial arch, therefore supplied by the facial nerve. All of them are inserted into the skin. *Topographically*, the muscles are grouped under the following six heads:

A. Muscles of the Scalp

Occipitofrontalis

B. Muscles of the Auricle

1. Auricularis anterior
2. Auricularis posterior
3. Auricularis superior

C. Muscles of the Eyelids

1. Orbicularis oculi

2. Corrugator supercilii

3. Levator palpebrae superioris (an extraocular muscle, supplied by the third cranial nerve)

D. Muscles of the Nose

1. Procerus
2. Compressor naris
3. Dilator naris
4. Depressor septi

E. Muscles Around the Mouth

1. Orbicularis oris
2. Levator labii superioris alaeque nasi
3. Zygomaticus major
4. Levator labii superioris
5. Levator anguli oris
6. Zygomaticus minor
7. Depressor anguli oris
8. Depressor labii inferioris
9. Mentalis
10. Risorius
11. Buccinators

F. Muscles of the Neck: Platysma (Fig. 1.1)

Functionally, most of the muscles may be regarded primarily as regulators of three opening situated on the face, namely the palpebral fissures, the nostrils and the oral fissures. Each opening has a single sphincter

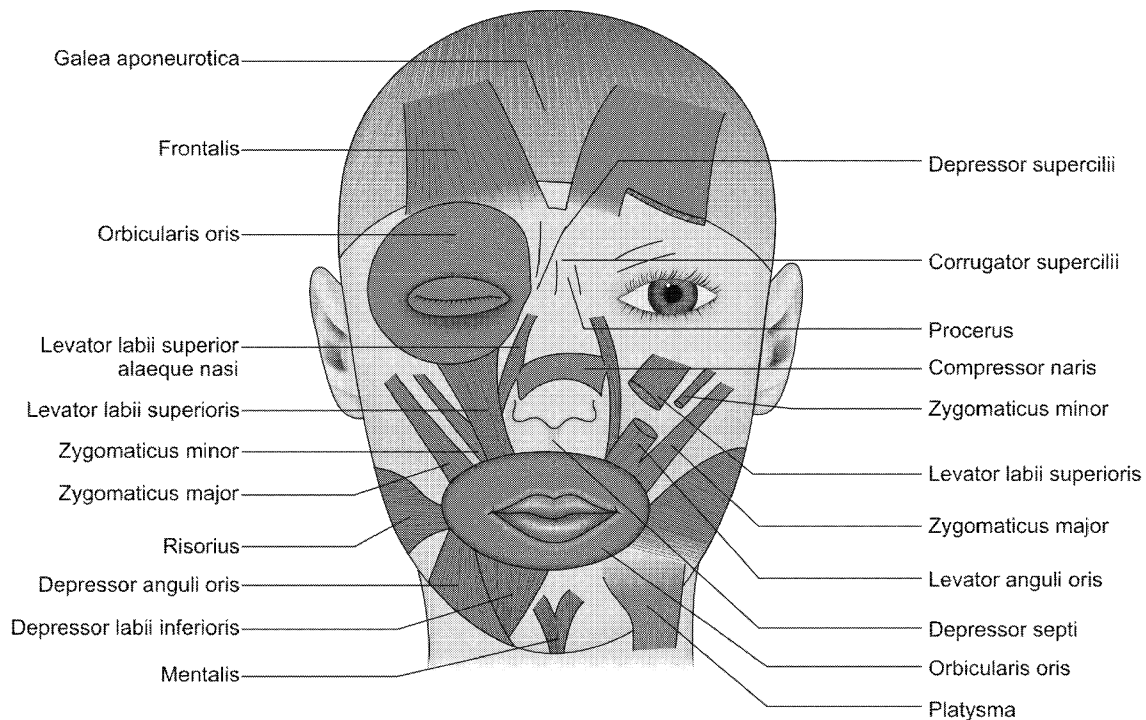


Fig. 1.1: Showing all the facial muscles

and a variable number of dilators. Sphincters are naturally circular and the dilators radial in their arrangement. A few common facial expressions and the muscles producing them are given below:

1. *Smiling and laughing*: Zygomaticus major
2. *Sadness*: Levator labii superioris and levator anguli oris
3. *Grief*: Depressor anguli oris
4. *Anger*: Dilator naris and depressor septi
5. *Frowning*: Corrugator supercilii and procerus
6. *Horror, terror and fright*: Platysma
7. *Surprise*: Frontalis
8. *Doubt*: Mentalis
9. *Grinning*: Risorius
10. *Contempt*: Zygomaticus minor
11. *Closing the mouth*: Orbicularis oris
12. *Whistling*: Buccinators and orbicularis oris

Clinically, the facial nerve is examined by testing the following facial muscles:

1. *Frontalis*: Ask the patient to look upwards without moving his head and look for the normal horizontal wrinkles of the forehead.
2. *Corrugator supercilii*: Frowning and making vertical wrinkles of the forehead.
3. *Orbicularis oris*: Whistling and pursing the mouth.
4. *Orbicularis oculi*: Tight closure of the eyes.
5. *Dilators of mouth*: Showing the teeth.
6. *Buccinators*: Puffing the mouth and then blowing forcibly as in whistling.
7. *Platysma*: Forcible pulling of the angles of the mouth downwards and backwards forming prominent vertical folds of skin on the side of the neck. The platysma contracts along with the risorius.

Q. 4. Write a short note on blood and nerve supply of the face. (TNMGR, March 2010)

Ans.

1. **Arterial supply**
 - a. Facial artery
 - b. Transverse facial artery
 - c. Arteries accompanying cutaneous nerves
2. **Veins of the face**
 - a. Facial vein
 - b. Retromandibular vein
3. **Lymphatics**
 - a. Preauricular lymph nodes
 - b. Submandibular lymph nodes
 - c. Submental lymph nodes

4. Nerve supply

- a. *Motor*—facial nerve and its branches
- b. *Sensory*—trigeminal and its branches; greater auricular nerve.

Q. 5. Write in detail about the external carotid artery and its branches. (TNMGR, Oct. 2003; Sept. 2008)

Ans. External carotid artery (ECA) lies anterior to the internal carotid artery and is the chief artery of supply to structures in the front of the neck and in the face.

Course and Relation

1. The external carotid artery begins in the carotid triangle at the level of the upper border of the thyroid cartilage. It runs upwards and slightly backwards and laterally and terminates behind the neck of the mandible by dividing into the maxillary and superficial temporal arteries.
2. The external carotid artery has a slightly curved course, so that it is anteromedial to the internal carotid artery in its lower part and anterolateral in its upper part.
3. In the carotid triangle, the external carotid artery lies under cover of the anterior border of the sternocleidomastoid. The artery is crossed superficially by the cervical branch of the facial nerve, the hypoglossal nerve, and the facial, lingual and superior thyroid veins. Deep to the artery, there are:
 - a. The wall of the pharynx
 - b. The superior laryngeal nerve
 - c. The ascending pharyngeal artery
4. Above the carotid triangle, the external carotid artery lies deep in the substance of the parotid gland. Within the gland, it is related superficially to the retromandibular vein and the facial nerve. Deep to the external carotid artery, there are:
 - a. The internal carotid artery
 - b. Styloglossus, stylopharyngeus, 9th nerve, pharyngeal branch of 10th, and styloid process.
 - c. The superior laryngeal nerve and the superior cervical sympathetic ganglion.

Branches

Anterior

- a. Superior thyroid
- b. Lingual
- c. Facial

Posterior

- a. Occipital
- b. Posterior auricular

Medial

- a. Ascending pharyngeal

Terminal

- a. Maxillary
- b. Superficial temporal

Superior thyroid artery: The superior thyroid artery arises from the external carotid artery just below the level of the greater cornua of the hyoid bone. It runs downwards and forwards parallel and just superficial to the external laryngeal nerve. It passes deep to the three long infrahyoid muscles to reach the upper pole of the lateral lobe of the thyroid gland. The artery and external laryngeal nerve are close to each other higher up, but diverge slightly near the gland. To avoid injury to the nerve, the superior thyroid artery is ligated as near the gland as possible.

Branches: (i) Terminal branch to the thyroid gland, (ii) superior laryngeal artery, (iii) sternocleidomastoid branch and (iv) cricothyroid branch.

Lingual artery (TNMGR, Oct. 2003): The lingual artery arises from the external carotid artery opposite the tip of the greater cornua of the hyoid bone. Its course is divided into three parts by the hyoglossus muscle. The *first part* lies in the carotid triangle. It forms a characteristic upward loop which is crossed by the hypoglossal nerve. The lingual loop permits free movements of the hyoid bone. The *second part* lies deep to the hyoglossus along the upper border of hyoid bone. It is superficial to the middle constrictor of the pharynx. The *third part* is called the *arteria profunda linguae*, or the *deep lingual artery*. It runs upwards along the anterior border of the hyoglossus, and then horizontally forwards on the undersurface of the tongue as the *fourth part*. In its vertical course, it lies between the genioglossus medially and the inferior longitudinal muscle of the tongue laterally. The horizontal part of the artery is accompanied by the lingual nerve. During surgical removal of the tongue, the first part of the artery is ligated before it gives any branch to the tongue or to the tonsil.

Facial artery (RGUHS, May 2011; KUHS, July 2012): The facial artery arises from the external carotid just above the tip of the greater cornua of the hyoid bone. It runs upwards first in the neck as *cervical part* and then on the face as *facial part*. The course of the artery in both places is tortuous. The tortuosity in the neck allows free movements of the pharynx during deglutition. On the face, it allows free movements of the mandible, the lips and the cheek during mastication and during various facial expressions.

1. **Cervical part:** It runs upwards on the superior constrictor of pharynx deep to the posterior belly of digastric with the stylohyoid and to the ramus of the mandible. It grooves the posterior border of the submandibular salivary gland. Next the artery makes an S-bend, first winding down over the submandibular gland and then up over the base of the mandible.

Branches: (i) Ascending palatine, (ii) tonsillar, (iii) sub-mental and (iv) glandular branches for the submandibular salivary gland and lymph nodes.

2. **Facial part:** It enters the face at anteroinferior angle of masseter muscle (here it is called *anesthetist's artery*), runs upwards close to angle of mouth, side of nose till medial angle of eye.

Branches: (i) Inferior labial, (ii) superior labial and (iii) lateral nasal.

Occipital artery: It arises from the posterior aspect of the external carotid artery, opposite the origin of the facial artery. It is crossed at its origin by the hypoglossal nerve. In the carotid triangle, the artery gives two *sternocleidomastoid branches*. The upper branch accompanies the accessory nerve and the lower branch arises near the origin of the occipital artery.

Posterior auricular artery: It arises from the posterior aspect of the external carotid artery just above the posterior belly of digastric. It runs upwards and backwards deep to the parotid gland but superficial to the styloid process. It crosses the base of the mastoid process and ascends behind the auricle. It supplies the back of the auricle, the skin over the mastoid process and over the back of the scalp. It is cut in incisions for the mastoid operations. Its *stylomastoid branch* enters the stylomastoid foramen and supplies the middle ear, the mastoid antrum and air cells, the semicircular canals and the facial nerve.

Ascending pharyngeal artery: This is a small branch that arises from the medial side of the external carotid artery. It arises very close to the lower end of external carotid artery. It runs vertically upwards between the side wall of the pharynx and the tonsil, medial wall of the middle ear and the auditory tube. It sends meningeal branches into the cranial cavity through the foramen lacerum, the jugular foramen and the hypoglossal canal.

Maxillary artery: This is the larger terminal branch of the external carotid artery. It begins behind the neck of the mandible under cover of the parotid gland. It runs forwards deep to the neck of the mandible below the auriculotemporal nerve and enters the infra-temporal fossa.

Superficial temporal artery: It is the smaller terminal branch of the external carotid artery. It begins behind the neck of the mandible under cover of the parotid gland.

- It runs vertically upwards, crossing the root of the zygoma, divides into anterior and posterior branches which supply the temple and scalp. The anterior branch anastomoses with the supraorbital and supratrochlear branches of the ophthalmic artery.
- In addition, it gives off a transverse facial artery and a middle temporal artery which runs on the temporal fossa deep to the temporalis muscle.

Q. 6. Write a note on maxillary artery.

(TNMGR, Sept. 2002; MAHE, April 2013)

Ans. This is the larger terminal branch of the external carotid artery, given off behind the neck of the mandible. It has a wide territory of distribution and supplies:

- External and middle ears and the auditory tube
- Dura mater
- Upper and lower jaws and teeth
- Muscles of the temporal and infratemporal regions
- Nose and paranasal air sinuses
- Palate
- Root of the pharynx

Course and Relations: Three Parts

- First (mandibular) part:** Runs horizontally forwards, first between the neck of the mandible and the sphenomandibular ligament, below the auriculo-temporal nerve and then along the lower border of the lateral pterygoid.
- Second (pterygoid) part:** Runs upwards and forwards superficial to the lower head of the lateral pterygoid.
- Third (pterygopalatine) part:** Passes between the two heads of the lateral pterygoid and through the pterygomaxillary fissure, to enter the pterygopalatine fossa.

Branches of First Part of the Maxillary Artery

- Deep auricular artery:** Supplies the external acoustic meatus, outer surface of the tympanic membrane and the temporomandibular joint.
- Anterior tympanic branch:** Supplies the middle ear, medial surface of the tympanic membrane.
- Middle meningeal artery:** Supplies bone, meninges, 5th, 7th nerves, middle ear and tensor tympani.
- Accessory meningeal artery:** It supplies meninges and structures in the infratemporal fossa.
- Inferior alveolar artery:** Supplies tongue, mylohyoid muscle, mandible, roots of mandibular teeth and chin.

Branches of Second Part of the Maxillary Artery

- Masseteric:** Masseter muscle.
- Deep temporal (anterior and posterior):** Temporalis muscle.
- Pterygoid:** Lateral and medial pterygoid muscle.
- Buccal:** Buccinator muscle.

Branches of Third Part of the Maxillary Artery

- Posterior superior alveolar artery:** Maxillary molar and premolar teeth; gums and maxillary air sinus.
- Infraorbital artery:** Orbital branches—orbit; middle superior alveolar branch—premolar teeth; anterior superior alveolar branches—incisor and canine teeth. Also branches to lacrimal sac, the nose and the upper lip.
- Greater palatine artery:** Soft palate, tonsil, palatine glands and mucosa; upper gums.
- Pharyngeal branch:** Roof of nose and pharynx; auditory tube; sphenoidal sinus.
- Artery of the pterygoid canal:** Auditory tube; upper pharynx and middle ear.
- Sphenopalatine artery (artery of "epistaxis"):** Lateral and medial walls of nose and paranasal sinuses.

Q. 7. Write a short note on pterygoid venous plexus.

(Bangalore Uni., Jan. 1992)

Ans. It lies around and within the lateral pterygoid muscle. The tributary of the plexus corresponds to the branches of the maxillary artery. The plexus is drained by the maxillary vein which begins at the posterior end of the plexus and unites with the superficial temporal vein to form the retromandibular vein. Thus, the maxillary vein accompanies only the first part of the maxillary artery.

The Plexus Communicates

- With the inferior ophthalmic vein through the inferior orbital fissure.
- With the cavernous sinus through the emissary vein.
- With the facial vein through the deep facial vein.

3. TEMPOROMANDIBULAR JOINT AND MUSCLES OF MASTICATION

Q. 1. Discuss the development of temporomandibular joint.

(BFUHS, May 2007)

Ans. At approximately 10 weeks the components of the fetus's future temporomandibular joint (TMJ) become evident in the mesenchyme between the condylar cartilage of the mandible and the developing temporal bone. Two slit-like joint cavities and an

intervening disc make their appearance in this region at 12 weeks. The mesenchyme around the joint begins to form the fibrous joint capsule. The developing superior head of the lateral pterygoid muscle attaches to the anterior portion of the fetal disk. The disk also continues posteriorly through the petrotympanic fissure and attaches to the malleus of the middle ear. This connection is usually obliterated by the growth of the lips of the petrotympanic fissure and does not exist in adult joint.

Q. 2. Describe in detail about the anatomy of the temporomandibular joint.

(TNMGR, March 2007, 2008; BFUHS, May 2010; May 2011; RGUHS, Nov. 2011; MUHS, April 2012; UHSR, April 2013)

Q. Write a short note on articular disc of temporomandibular joint.

(TNMGR, April 1998; March 2002; Sept. 2002)

Q. Describe the anatomy and development of TMJ. Discuss myofunctional pain dysfunction syndrome.

(Nagpur Uni., April 2002; RGUHS, 2006)

Q. Describe the temporomandibular joint, its relations, movements, age changes and disorders of the TMJ.

(RGUHS, Nov. 2011; KUHS, Jan. 2014; MUHS, April 2014)

Q. Describe the applied anatomy and physiology of the temporomandibular joint.

(RGUHS, 2006 and April 2007; BFUHS, Nov. 2011; KUHS, June 2013)

Q. Enumerate the various temporomandibular joint ligaments along with their role.

(TNMGR, Oct. 2003; BFUHS, Oct. 2010)

Q. Briefly describe development, anatomy and histological characteristics of TMJ.

(BFUHS, May 2009)

Q. Give classification of joints. Describe the temporomandibular joint and discuss how it differs from other joints?

(MUHS, November 2014)

Ans. Classification of joints: Joint is a junction between two or more bones or cartilages.

a. Structural classification

1. **Fibrous joint:** (i) Sutures, (ii) syndesmosis and (iii) gomphosis.
2. **Cartilaginous joints:** (i) Primary cartilaginous joint or synchondrosis, (ii) secondary cartilaginous joints or symphysis.
3. **Synovial joints:** (i) Ball and socket or spheroidal joint, (ii) sellar or saddle joints, (iii) condylar or bicondylar joints, (iv) ellipsoid joints, (v) hinge joints, (vi) pivot or trochoid joints and (vii) plane joints.

b. Functional classification (according to the degree of mobility):

1. Synarthrosis (immovable), like fibrous joints.
2. Amphiarthrosis (slightly movable), like cartilaginous joints.
3. Diarthrosis (freely movable), like synovial joints.

TMJ: This is a synovial joint of the condylar variety (Fig. 1.2).

Articular surfaces: The upper articular surface is formed by the following parts of the temporal bone:

- a. Articular tubercle.
- b. Anterior part of mandibular fossa.

The inferior articular surface is formed by the head of mandible.

The articular surfaces are covered with fibrocartilage. The joint cavity is divided into upper and lower parts by an intra-articular disc.

Ligaments: Ligaments are the fibrous capsules, the lateral ligament, the sphenomandibular ligament and the stylomandibular ligament.

1. The **fibrous capsule** is attached above to the articular tubercle, the circumference of the mandibular fossa and the squamotympanic fissure and below to the neck of the mandible. The capsule is loose above the intra-articular disc, and tight below it. The synovial membrane lines the fibrous capsule and the neck of the mandible.
2. The **lateral or temporomandibular ligament** reinforces and strengthens the lateral part of the capsular ligament. Its fibers are directed downwards and backwards. It is attached above to the articular tubercle, and below to the posterolateral aspect of the neck of the mandible.

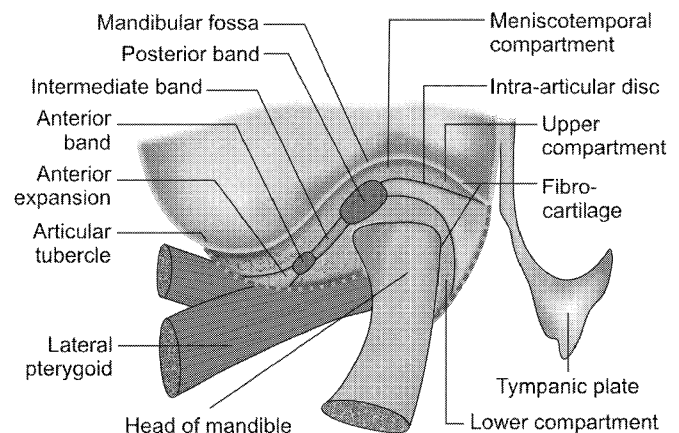


Fig. 1.2: TMJ and articular disc with their attachments

3. The **sphenomandibular ligament** is an accessory ligament that lies on a deep plane away from the fibrous capsule. It is attached superiorly to the spine of the sphenoid, and inferiorly to the Lingula of the mandibular foramen. It is a remnant of the dorsal part of Meckel's cartilage. The ligament is related laterally to:

- a. Lateral pterygoid muscle
- b. Auriculotemporal nerve
- c. Maxillary artery

The ligament is related medially to:

- a. Chorda tympani
- b. Wall of pharynx

4. The **stylomandibular ligament** is another accessory ligament of the joint. It represents a thickened part of the deep cervical fascia which separates the parotid and submandibular glands. It is attached above to the lateral surface of the styloid process and below to the angle and adjacent part of the posterior border of the ramus of mandible.

Synovium: The capsule is lined with synovium and the joint cavity is filled with synovial fluid. Synovial tissue is a vascular connective tissue lining the fibrous joint capsule and extending to the boundaries of the articulating surfaces. Synovial fluid is a filtrate of plasma with added mucins and proteins. Its main constituent is hyaluronic acid. Fluid forms on the articulating surfaces, decreasing friction during joint compression and motion.

Articular disc: The articular disc is an oval fibrous plate that divides the joint into upper and lower compartments. The upper compartment permits gliding movements and the lower, rotator as well as gliding movements. The disc has a concavo-convex superior surface, and a concave inferior surface. The periphery of the disc is attached to fibrous capsule. The disc is composed of an anterior extension, anterior thick band, intermediate zone, posterior thick zone and bilaminar region. The disc represents the degenerated primitive insertion of lateral pterygoid.

Histology

1. **Bony structure:** The condyle of mandible is composed of cancellous bone covered by a thin layer of compact bone. The red marrow in the condyle is of myeloid or cellular type. The roof of the glenoid fossa consists of a thin, compact layer of bone. The articular eminence is composed of spongy bone covered with a thin layer of compact bone.
2. **Articular disc:** The articular disc is composed of dense fibrous tissue, with a few elastic fibers.

3. **Synovial membrane:** The articular capsule is lined with synovial membrane that folds to form synovial villi into the joint spaces. The synovial membrane consists of internal cells and subintimal connective tissue layer. The internal cells are fibroblast like (B cell), macrophage like (A cell), and cellular morphology between A and B cell.

Relations of Temporomandibular Joint

Lateral

- a. Skin and fasciae
- b. Parotid gland
- c. Temporal branches of the facial nerve

Medial

- a. Tympanic plate
- b. Spine of the sphenoid
- c. Auriculotemporal and chorda tympani nerves
- d. Middle meningeal artery

Anterior

- a. Lateral pterygoid
- b. Masseteric nerve and artery

Posterior

- a. Parotid gland
- b. Superficial temporal vessels
- c. Auriculotemporal nerve

Superior

- a. Middle cranial fossa
- b. Middle meningeal vessels

Inferior

Maxillary artery and vein.

Blood supply: Superficial temporal and maxillary arteries. Veins follow the arteries.

Nerve supply: Auriculotemporal nerve and masseteric nerve.

Movements of TMJ

1. **Forward movement or protrusion** of the mandible: The articular disc glides forwards over the upper articular surface, the head of the mandible moving with it.
2. **Retraction:** The articular disc glides backwards over the upper articular surface taking the head of mandible with it.
3. **Slight opening of the mouth or depression of the mandible:** The head of the mandible moves on the undersurface of the disc like a hinge.

4. **Wide opening of the mouth:** Hinge-like movement is followed by gliding of the disc and the head of the mandible, as in protraction. At the end of this movement, the head comes to lie under the articular tubercle.
5. **Closing the mouth or elevation of the mandible:** Reverse of that in opening.
6. **Chewing movements:** Involve side to side movements of the mandible. In these movements, the head of right side glides forwards along with the disc as in protraction, but the head of the left side merely rotates on a vertical axis. As a result of this, the chin moves forward and to left side. Alternate movements of this kind on the two sides result in side to side movements of the jaw.

Muscles Producing Movements

1. **Depression:** Lateral pterygoid muscle. Digastrics, geniohyoid and mylohyoid muscles help when the mouth is opened wide or against resistance.
2. **Elevation:** Masseter, temporalis and the medial pterygoid muscles of both sides.
3. **Protrusion:** Lateral and medial pterygoids.
4. **Retraction:** Posterior fibers of the temporalis.
5. **Latent or side to side movements:** For example, turning the chin to left side produced by left lateral pterygoid and right medial pterygoid and vice versa.

Age Changes

1. The large marrow spaces in the condyle decrease in size with age.
2. The trabeculae become thickened.
3. The red marrow gets replaced by fatty marrow.
4. The fibrous layer covering the articulating surface shows calcification.

TMJ Disorders

- a. **Congenital and developmental:** Aplasia, hypoplasia, hyperplasia, etc.
- b. **Inflammatory:** Arthritis.
- c. **Articular disc related:** Deviation, disc displacement, dislocation.
- d. **Ankylosis:** True/false, bony/fibrous.
- e. Neoplasia.
- f. **Muscle related:** Myofascial pain, spasm.

Myofascial Pain Dysfunction Syndrome (MPDS)

It is characterized by:

1. Masticatory muscle tenderness (lateral pterygoid > temporalis > medial pterygoid > masseter).
2. Limited opening of mandible (<37 mm).
3. Joint sounds.

4. Seen more commonly in females.
5. It occurs due to spasm of the masticatory muscles.
6. It may be related to stress.
7. Treatment is conservative.

Q. 3. Describe the muscles of mastication under the following headings:

(KUHS, June 2013; UHSR, April 2015)

a. Attachments

b. Nerve supply and actions

c. Development

Q. Narrate the anatomy and functions of muscles of mastication.

(MUHS, May 2009; TNMGR, March 2009; April 2012; RGUHS, May 2012)

Ans. The muscles of mastication move the mandible during mastication and speech. They develop from the mesoderm of the first branchial arch and are supplied by the mandibular nerve which is the nerve of that arch. They are:

1. **Masseter:** Quadrilateral in shape covers lateral surface of mandible (Fig. 1.3).

Origin

- a. **Superficial layer (largest):** Anterior two thirds of lower border of zygomatic arch and adjoining zygomatic process of maxilla.
- b. **Middle layer:** Anterior two-thirds of deep surface and posterior one-third of lower border of zygomatic arch.
- c. **Deep layer:** Deep surface of zygomatic arch.

Fibers

- a. Superficial fibers pass downwards and backwards at 45°.
- b. Middle and deep fibers pass vertically downwards.

Insertion

- a. **Superficial layer:** Lower part of the lateral surface of ramus of mandible.

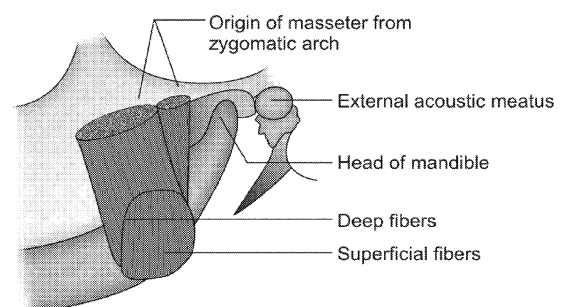


Fig. 1.3: Origin and insertion of masseter muscle

b. *Middle layer*: Middle part of the ramus.

c. *Deep layer*: Rest of the ramus of mandible.

Nerve supply: Masseteric nerve.

Action: Elevates mandible to close the mouth to bite.

2. *Temporalis*: Fan-shaped (Fig. 1.4).

Origin

a. Temporal fossa, excluding zygomatic bone.

b. Temporal fascia.

Fibers: Anterior fibers run vertically, middle obliquely and posterior horizontally. All converge and pass through gap deep to zygomatic arch.

Insertion

a. Margins and deep surface of coronoid process.

b. Anterior border of ramus of mandible.

Nerve supply: Deep temporal branches from anterior division of mandibular nerve.

Actions

1. Elevates mandible.
2. Helps in side to side grinding movements.
3. Posterior fibers retract the protruded mandible.

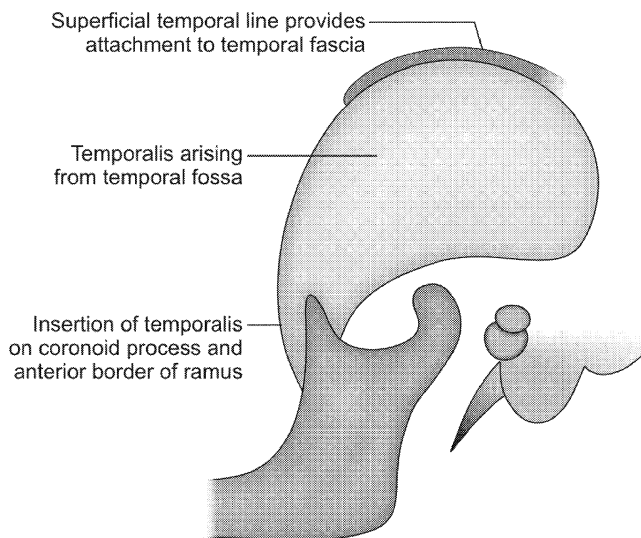


Fig. 1.4: Origin and insertion of temporalis muscle

3. *Lateral pterygoid*: Short and conical (Fig. 1.5).

Origin

a. *Upper head (small)*: Infratemporal surface and crest of greater wing of sphenoid bone.

b. *Lower head (larger)*: Lateral surface of lateral pterygoid plate.

Fibers: Run backwards, laterally and converge for insertion.

Insertion

a. Pterygoid fovea on the anterior surface of neck of mandible.

b. Anterior margin of articular disc and capsule of temporomandibular joint.

Nerve supply: A branch from anterior division of mandibular nerve.

Actions

1. Depress mandible to open mouth, with suprahyoid muscle.
2. Lateral and medial pterygoids protrude mandible.
3. Left lateral pterygoid and right medial pterygoid turn the chin to left side as part of grinding movements.

Relations of Lateral Pterygoid

Superficial: Masseter, ramus of mandible, tendon of the temporalis, maxillary artery.

Deep: Mandibular nerve, middle meningeal artery, sphenomandibular ligament, deep head of the medial pterygoid.

Structures emerging at the upper border: Deep temporal nerves, masseteric nerve.

Structures emerging at the lower border: Lingual nerve, inferior alveolar nerve, middle meningeal artery passes upwards deep to it.

Structures passing through the gap between the two heads: Maxillary artery enters the gap. The buccal branch of the mandibular nerve comes out through gap. The pterygoid plexus of vein surrounds the lateral pterygoid.

4. *Medial pterygoid*: Quadrilateral in shape (Fig. 1.5).

Origin

a. *Superficial head*: Maxillary tuberosity and adjoining bone.

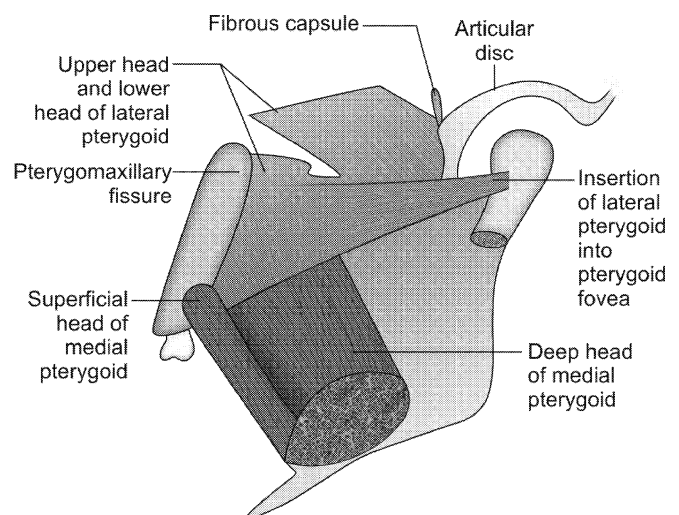


Fig. 1.5: Origin and insertion of lateral and medial pterygoid muscle

b. *Deep head (large)*: Medial surface of lateral pterygoid plate and adjoining process of palatine bone.

Fibers: It runs downwards, backwards and laterally.

Insertion: Medial surface of the angle and adjoining ramus of the mandible.

Nerve supply: Nerve to medial pterygoid.

Actions:

1. Elevates mandible.
2. Helps protrude mandible.
3. Right medial pterygoid with left lateral pterygoid turn the chin to left side.

Relations of Medial Pterygoid

Superficial relations: The upper part of muscle is separated from the lateral pterygoid muscle—lateral pterygoid plate, lingual nerve, and inferior alveolar nerve. Lower down the muscle is separated from the ramus of mandible by the lingual and inferior alveolar nerves, the maxillary artery, and the sphenomandibular ligament.

Deep relations: Tensor veli palatini, superior constrictor of pharynx, styloglossus, stylopharyngeus attached to the styloid process.

4. TONGUE AND PALATE

Q. 1. Describe the tongue. Add notes on its blood supply, nerve supply, lymphatic drainage, microscopic structure and embryonic development.

(TNMGR, Sept. 2007; March, Sept. 2009; MUHS, May 2011; KUHS, June 2013; Jan. 2014)

Q. Write a short note on taste buds.

(TNMGR, Sept. 2009; April 2013)

Ans. The tongue is a muscular organ situated in the floor of the mouth. It is associated with the functions of taste, speech, mastication and deglutition.

External features: The tongue has:

1. A root.
2. A tip.
3. A body, which has:
 - A curved upper surface or dorsum.
 - An inferior surface.

The **dorsum** is divided into oral and pharyngeal parts. The inferior surface is confined to the oral part only.

The **root** is attached to the mandible and soft palate above, and to the hyoid bone below.

The **tip** of the tongue forms the anterior free end which, at rest, lies behind the upper incisor teeth.

The dorsum of the tongue is convex in all directions. It is divided into:

- a. An oral part or anterior two-thirds.
- b. A pharyngeal part or posterior one-third, by a faint V-shaped groove, the sulcus terminalis. The two limbs of the 'V' meet at a median pit, named the *foramen caecum*. They run laterally and forward up to the palatoglossal arches. The foramen caecum represents the site from which the thyroid diverticulum grows down in the embryo.

The **oral or papillary** part of the tongue is placed on the floor of the mouth. In front of the palatoglossal arch, each margin shows 4 to 5 vertical fold called the foliate papillae.

The superior surface of the oral part shows a median furrow and is covered with papillae. The inferior surface is covered with a smooth mucous membrane, which shows a median fold called *frenulum linguae*. On the either side of the frenulum, there is a prominence produced by the deep lingual veins. More laterally there is a fold called the *plica fimbriata* that is directed forwards and medially towards the tip of the tongue.

The **pharyngeal or lymphoid** part of the tongue lies behind the palatoglossal arches and the sulcus terminalis. Its posterior surface, sometimes called the base of the tongue, forms the anterior wall of the oropharynx. The mucous membrane has no papillae, but has many lymphoid follicles that collectively constitute the **lingual tonsil**. Mucous glands are also present.

The **posteriormost part** of the tongue is connected to the epiglottis by three folds of mucous membrane. These are median glossoepiglottic fold and the right and left lateral glossoepiglottic folds. On either side of the median fold, there is a depression called the *vallecula*. The lateral folds separate the vallecula from the piriform fossa.

Papillae of the tongue: These are projections of mucous membrane or corium which give the anterior two-thirds of the tongue its characteristic roughness. These are of the following types (Fig. 1.6):

- i. **Vallate or circumvallate papillae**: They are large in size 1–2 mm in diameter and are 8–12 in number. They are situated immediately in front of the sulcus terminalis. Each papilla is a cylindrical projection surrounded by a circular sulcus. The walls of the papilla are raised above the surface.
- ii. **Fungiform papillae**: They are numerous near the tip and margins of tongue, but some of them are also scattered over the dorsum. These are smaller than the vallate papillae, but larger than the filiform

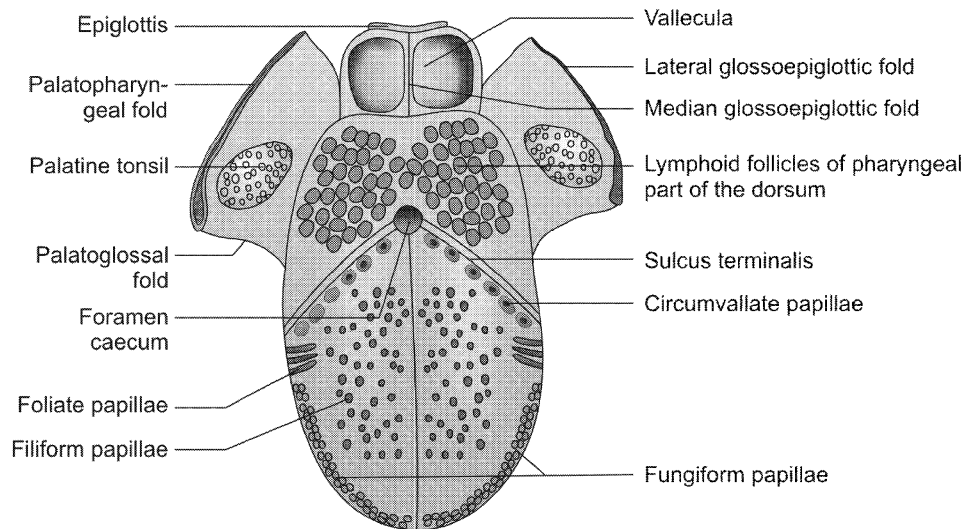


Fig. 1.6: Dorsum of tongue showing papillae, epiglottis and palatine tonsil

papillae. Each papilla consists of a narrow pedicle and a large rounded head. They are distinguished by their bright red colour.

- iii. **Filiform papillae or conical papillae:** They cover the presulcal area of the dorsum of the tongue, and give it a characteristic velvety appearance. They are the smallest and most numerous of the lingual papillae. Each is pointed and covered with keratin; the apex is often split into filamentous processes.
- iv. Few **foliate papillae** are also present.

Muscles of the tongue: A middle fibrous septum divides the tongue into right and left halves. Each half contains four intrinsic and four extrinsic muscles.

Intrinsic muscles

1. Superior longitudinal
2. Inferior longitudinal
3. Transverse
4. Vertical

Extrinsic muscles

- | | |
|-----------------|------------------|
| 1. Genioglossus | 2. Hyoglossus |
| 3. Styloglossus | 4. Palatoglossus |

The intrinsic muscles occupy the upper part of the tongue and are attached to the sub mucous fibrous layer and to the median fibrous septum. They alter the shape of the tongue.

The **superior longitudinal muscle** lies beneath the mucous membrane. It shortens the tongue and makes its dorsum concave.

The **inferior longitudinal muscle** is a narrow band lying close to the inferior surface of the tongue between

the genioglossus and the hyoglossus. It shortens the tongue and makes its dorsum convex.

The **transverse muscle** extends from the median septum to the margins. It makes the tongue narrow and elongated.

The **vertical muscle** is found at the borders of the anterior part of the tongue. It makes the tongue broad and flattened.

The **extrinsic muscles** connect the tongue to the mandible via genioglossus; to the hyoid bone through hyoglossus; to the styloid process via styloglossus, and the palate via palatoglossus. These are described as (see table on next page):

Arterial supply: Lingual artery, tonsillar and ascending pharyngeal artery.

Venous drainage: Deep lingual vein is the largest and principal vein of the tongue. All the veins unite at posterior border of the hyoglossus to form the lingual vein which ends in the internal jugular vein.

Lymphatic drainage

1. The tip of the tongue drains bilaterally to the submental nodes.
2. The right and left halves of the remaining part of the anterior two-thirds of the tongue drain unilaterally to the submandibular nodes.
3. The posterior one-third of the tongue drains bilaterally to the *jugulo-omohyoid nodes*; the *lymph nodes of the tongue*.
4. The posterior most part of the tongue drains bilaterally into the upper deep cervical lymph nodes.

Muscles	Origin	Insertion	Action
Palatoglossus	Oral surface of palatine aponeurosis.	Descends in the palatoglossal arch to the side of tongue at the junction of its oral and pharyngeal parts.	Pulls up the root of tongue, approximate the palatoglossal arches, closes the oropharyngeal isthmus.
Hyoglossus	Whole length of greater cornua and lateral part of the body of hyoid bone.	Side of tongue between styloglossus and inferior longitudinal muscle of the tongue.	Depresses tongue, makes dorsum convex, and retracts the protruded tongue.
Styloglossus	Tip and part of the anterior surface of styloid process.	Into the side of tongue.	Pulls tongue upwards and backwards.
Genioglossus	Upper genial tubercle of mandible.	Upper fibers into the tip of tongue. Middle fibers into dorsum. Lower fibers into hyoid bone.	Retracts the tongue. Depresses the tongue. Pulls the posterior part of tongue forwards and protrude the tongue forwards.

Nerve Supply

a. **Motor nerves:** All the intrinsic and extrinsic muscles, except palatoglossus, are supplied by the hypoglossal nerve. Palatoglossus is supplied by the cranial root of the accessory nerve through the pharyngeal plexus.

b. **Sensory nerves**

- **Lingual nerve:** General sensation.
- **Chorda tympani:** Taste for the anterior two-thirds of the tongue except vallate papillae.
- **Glossopharyngeal nerve:** Both general sensation and taste for the posterior one-third of the tongue including the circumvallate papillae.

The posterior most part of the tongue is supplied by the vagus nerve through the internal laryngeal branch.

Microscopic Structure of the Tongue

1. The bulk of tongue is made up of striated muscle.
2. The mucous membrane consists of layer of connective tissue, lined by stratified squamous epithelium. On the oral part, it is thin, forms papillae. On the pharyngeal part, it is rich in lymphoid follicles.

Q. 2. Write a note on hyoglossus muscle and its relations.

(TNMGR, Feb. 2005; KUHS, Dec. 2012; June 2013)

Ans. Relations of hyoglossus muscle

Superficial: Styloglossus, lingual nerve, submandibular ganglion, deep part of the submandibular gland, submandibular duct, hypoglossal nerve and veins accompanying it.

Deep

- a. Inferior longitudinal muscle of tongue
- b. Genioglossus

c. Middle constrictor of the pharynx

d. Glossopharyngeal nerve

e. Stylohyoid ligament

f. Lingual artery

Structures passing deep to posterior border of hyoglossus, from above downwards:

a. Glossopharyngeal nerve

b. Stylohyoid ligament

c. Lingual artery.

Q. 3. Describe the development of tongue.

(TNMGR, March 2008; KUHS, June 2013)

Ans. The tongue develops in relation to the pharyngeal arches in the floor of the developing mouth. Each pharyngeal arch arises as a mesodermal thickening in the lateral wall of the foregut and then it grows ventrally to become continuous with the corresponding arch of the opposite side. The medial-most parts of the mandibular arches proliferate to form two *lingual swellings*, partially separated from each other by another midline swelling, *tuberculum impar*. Immediately behind the tuberculum impar, the epithelium proliferates to form a down growth (*thyroglossal duct*) from which the thyroid gland develops. The site of this down growth is subsequently marked by a depression called the *foramen caecum*. Another midline swelling is seen in relation to the medial ends of the second, third and fourth arches. This swelling is called the *hypobranchial eminence*. The eminence soon shows a subdivision into a cranial part related to the second and third arches (called the *copula*) and a caudal part related to the 4th arch. The caudal part forms the epiglottis (Fig. 1.7).

The **anterior two-thirds** of the tongue is formed by fusion of:

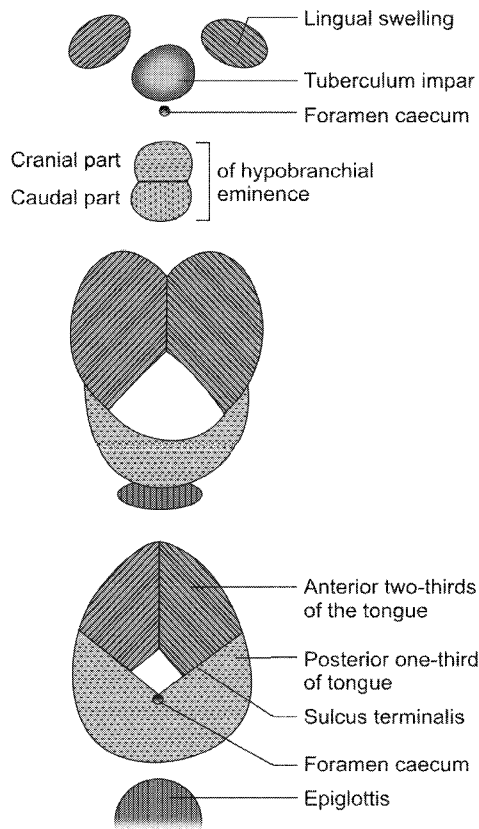


Fig. 1.7: Development of various parts of tongue

- a. The tuberculum impar.
- b. The two lingual swellings.

The **anterior two-thirds** of the tongue is thus derived from the mandibular arch.

The **posterior one-third** of the tongue is formed from the cranial part of the hypobranchial eminence (copula). In this situation, the second arch mesoderm gets buried below the surface. The third arch mesoderm grows over it to fuse with the mesoderm of the first arch. The posterior one-third of the tongue is thus formed by third arch mesoderm.

The **posteriormost** part of the tongue is derived from the fourth arch.

In keeping with its embryological origin, the anterior two-thirds of the tongue is supplied by the lingual branch of the mandibular nerve, which is the post-trematic nerve of the first arch and by the chorda tympani (pretrematic) which is the most posterior part of the tongue is supplied by the superior laryngeal nerve, which is the nerve of the fourth arch.

The **musculature** of the tongue is derived from the occipital myotomes. This explains its nerve supply by the hypoglossal nerve, which is the nerve of these myotomes.

The **epithelium** of the tongue is at first made up of a single layer of cells. Later it becomes stratified and papillae become evident. Taste buds are formed in relation to the terminal branches of the innervating nerve fibers. Development of the tongue starts in the 4th month of intrauterine life.

Developmental Anomalies of the Tongue

1. The tongue may be too large (**macroglossia**) or too small (**microglossia**). Very rarely the tongue may be absent (**aglossia**).
2. The tongue may be bifid because of non-fusion of the two lingual swellings.
3. The apical part of the tongue may be anchored to the floor of the mouth by an overdeveloped frenulum. This condition is called **ankyloglossia** or **tongue-tie**. It interferes with speech. Occasionally, the tongue may be adherent, to the palate (**ankyloglossia superior**).
4. A rhomboid-shaped smooth zone may be present on the tongue in front of the foramen caecum. It is considered to be the result of persistence of the tuberculum impar.
5. Thyroid tissue may be present in the tongue either under the mucosa or within the muscles.
6. The surface of the tongue may show fissures
7. Remnants of the thyroglossal duct may form cysts at the base of the tongue.

Q. 4. Write a short note on soft palate.

(TNMGR, April 1997)

Ans. It is a movable muscular fold, suspended from the posterior border of the hard palate. It separates the nasopharynx from the oropharynx. The soft palate has two surfaces, anterior and posterior, and two borders, superior and inferior.

The *anterior (oral)* surface is concave and is marked by a median raphe.

The *posterior surface* is convex, and is continuous superiorly with the floor of the nasal cavity. The *superior border* is attached to the posterior border of the hard palate, blending on each side with the pharynx.

The *inferior border* is free and bounds the pharyngeal isthmus. From its middle, there hangs a conical projection, called the *uvula*. From each side of the base of the uvula, two curved folds of mucous membrane extend laterally and downwards. The anterior fold is called the *palatoglossal arch* or *anterior pillar of fauces*. It contains the palatoglossus muscle and reaches the side of the tongue. The posterior fold is called the *palatopharyngeal arch* or *posterior pillar of fauces*. It contains the palatopharyngeus muscle. It forms the

posterior boundary of the tonsillar fossa, and merges inferiorly with the lateral wall of pharynx.

Structure: The soft palate is a fold of mucous membrane containing the following parts:

- **Palatine aponeurosis:** Flattened tendon of the tensor veli palatini forms the fibrous basis of the palate. Near

the median plane, the aponeurosis splits to enclose the musculus uvulae.

- **Levator veli palatini** and **palatopharyngeus** lie on the superior surface of the palatine aponeurosis. **Palatoglossus** lies on the inferior surface of the palatine aponeurosis.

Muscles of the Soft Palate

Muscles	Origin	Insertion	Action
Tensor veli palatini	Lateral side of auditory tube. Adjoining part of the base of the skull.	Posterior border of hard palate and inferior surface of palate.	Tightens the soft palate. Opens the auditory tube.
Levator veli palatini	Inferior aspect of auditory tube, and adjoining part of inferior surface of petrous temporal bone.	Upper surface of the palatine aponeurosis.	Elevates soft palate and closes the pharyngeal isthmus. Opens the auditory tube.
Musculus uvulae	Posterior nasal spine. Palatine aponeurosis.	Mucous membrane of uvula.	Pulls up the uvulae.
Palatoglossus	Oral surface of palatine aponeurosis.	Side of the tongue.	Pulls up the root of the tongue, closes the oropharyngeal isthmus.
Palatopharyngeus	Anterior fasciculus: From posterior border of hard palate. Posterior fasciculus: From the palatine aponeurosis.	Posterior border of the lamina of the thyroid cartilage. Wall of the pharynx and its median raphe.	Pulls up the wall of the pharynx and shortens it during swallowing.

Nerve Supply

1. **Motor nerves:** All muscles of the soft palate except the tensor veli palatini are supplied by the pharyngeal plexus. The tensor veli palatini is supplied by the mandibular nerve.
2. **General sensory nerves**
 - a. The middle and posterior lesser palatine nerves.
 - b. The glossopharyngeal nerve.
3. **Special sensory or gustatory nerves:** Lesser palatine nerves.
4. **Secretomotor nerves:** Lesser palatine nerves.

Passavant's ridge: Some of the upper fibers of the palatopharyngeus pass circularly deep to the mucous membrane of the pharynx, and form a sphincter internal to the superior constrictor. These fibers constitute Passavant's muscle which on contraction raises a ridge called the *Passavant's ridge* on the posterior wall of the nasopharynx. When the soft palate is elevated it comes in contact with this ridge, the two together closing the pharyngeal isthmus between the oropharynx and the nasopharynx.

Movements and Functions of the Soft Palate

1. It isolates the mouth from the oropharynx during chewing, so that breathing is unaffected.
2. It separates the oropharynx from the nasopharynx by locking into Passavant's ridge during the second stage of swallowing, so that food does not enter the nose.

3. By varying the degree of closure of the pharyngeal isthmus, the quality of voice can be modified and various consonants correctly pronounced.
4. During sneezing, the blast of air is appropriately divided and directed through the nasal and oral cavities without damaging the narrow nose.
5. During coughing, it directs air and sputum into the mouth and not into the nose.

Blood Supply

Arteries

1. Greater palatine branch of maxillary artery.
2. Ascending palatine branch of facial artery.
3. Palatine branch of ascending pharyngeal artery.

Veins: Pterygoid and tonsillar plexuses of veins.

Lymphatics: Upper deep cervical and retropharyngeal lymph nodes.

Q. 5. Write about development of hard and soft palate and its anomalies.

(TNMGR, March 2007; KUHS, June 2013; RUHS, June 2014)

Ans. Maxillary processes not only form the upper lip but also extend backwards on either side of the stomatodaeum. From each maxillary process, a plate-like shelf grows medially. This is called the *palatal process*. The palate is formed from three components (Fig. 1.8). These are:

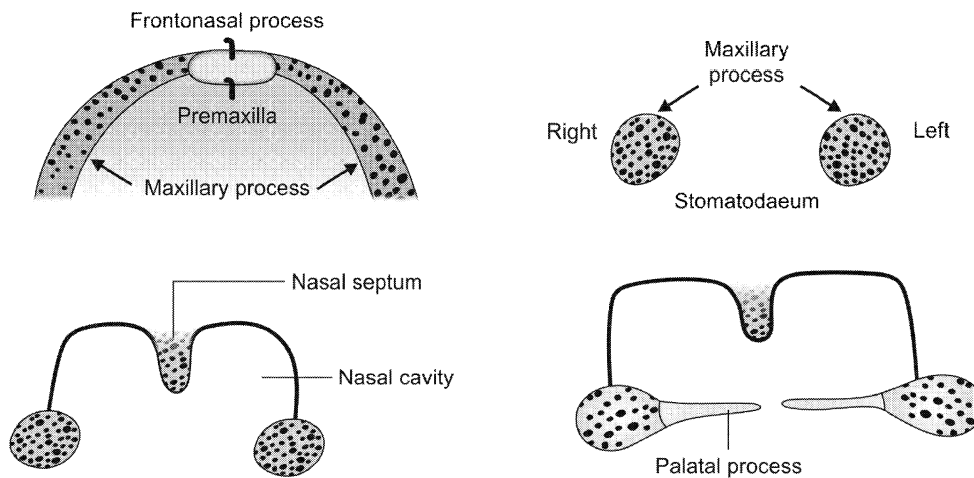


Fig. 1.8: Development of palate (hard and soft)

1. The two palatal processes.
2. The primitive palate formed from the frontonasal process.
 - a. Each palatal process fuses with the posterior margin of the primitive palate .
 - b. The two palatal processes fuse with each other in the midline. Their fusion begins anteriorly and proceeds backwards.
 - c. The medial edges of the palatal processes fuse with the lower edge of the nasal septum, thus separating two nasal cavities from each other and from the mouth.

At a later stage, the mesoderm in the palate undergoes intramembranous ossification to form the *hard palate*. However, ossification does not extend into the most posterior portion, which remains as the *soft palate*. The part of the palate derived from the frontonasal process forms the *premaxilla*, which carries the incisor teeth.

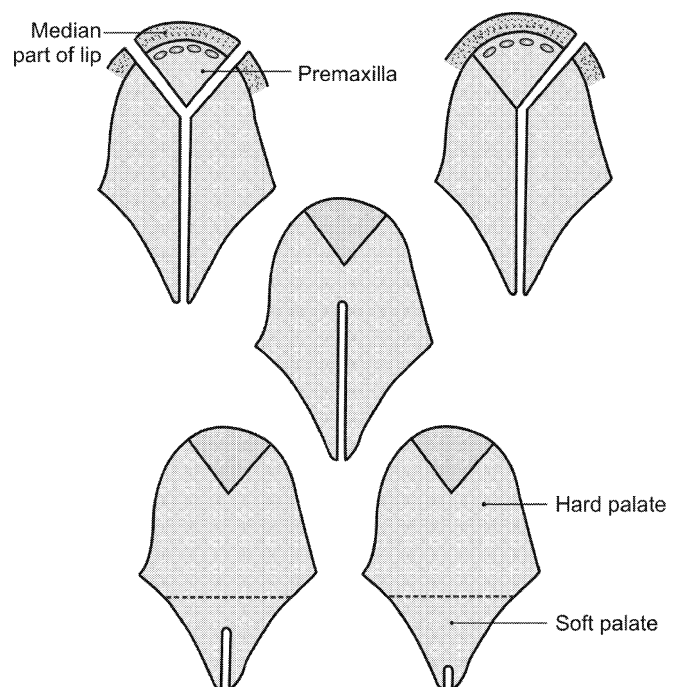


Fig. 1.9: Types of cleft palate

Developmental Anomalies (TNMGR, April 2012)

Cleft palate: Defective fusion of the various components of the palate gives rise to clefts in the palate. Clefts of the palate that extend to its anterior end are associated with harelip. As both the upper lip and the palate are formed by fusion of the maxillary processes with the frontonasal process. They result in anomalous communications between the mouth and the nose. These may be unilateral or bilateral (Fig. 1.9).

Q. 6. Write a short note on development of palatine tonsil. (TNMGR, March 2007)

Ans. The palatine tonsil develops (on each side) in relation to the lateral part of the second pharyngeal

pouch. The endoderm lining the pouch undergoes considerable proliferation. As a result, most of the pouch is obliterated. Lymphocytes collect in relation to the endodermal cells. The intratonsillar cleft or tonsillar fossa is believed to represent a persisting part of the second pharyngeal pouch. Similar epithelial proliferations and aggregations of lymphoid tissue give rise to the tubal tonsils, the lingual tonsil and the pharyngeal tonsils.

Q. 7. Write short note on palatine tonsil.

(TNMGR, April 1995; Feb. 2005)

Ans. Palatine tonsil (the tonsil) occupies the tonsillar fossa between the palatoglossal and palatopharyngeal arches. It has *two surfaces*, medial and lateral; *two borders*, anterior and posterior and *two poles*, upper and lower.

The *medial surface* covered by stratified squamous epithelium continuous, has 12 to 15 crypts. The largest of these is called the *intratonsillar cleft*.

The *lateral surface* covered by a sheet of fascia which forms the capsule of the tonsil. It is loosely attached to the muscular wall of the pharynx, formed by the superior constrictor and the styloglossus, but anteroinferiorly the capsule is firmly adherent to the side of the tongue just in front of the insertion of the palatoglossus and the palatopharyngeus muscles. This firm attachment keeps the tonsil in place during swallowing. The tonsillar artery enters the tonsil by piercing the superior constrictor.

The palatine vein or external palatine or paratonsillar vein descends from the palate in the loose areolar tissue on the lateral surface of the capsule. The bed of the tonsil is formed from within outwards by:

- a. The pharyngobasilar fascia.
- b. The superior constrictor and palatopharyngeus muscles.
- c. The buccopharyngeal fascia.
- d. The styloglossus.
- e. The glossopharyngeal nerve.

The *anterior border* related to the palatoglossal arch with its muscle.

The *posterior border* related to the palatopharyngeal arch with its muscle.

The *upper pole* related to the soft palate and the lower pole, to the tongue.

Microscopic structures: Each palatine tonsil consists of diffuse lymphoid tissue, covered by stratified squamous epithelium, which extends into the substance of tonsil in the form of tonsillar crypts. Numerous mucous glands open into the crypts.

Arterial Supply

1. Tonsillar branch of facial artery.
2. *Additional sources*
 - a. Ascending palatine branch of facial artery.
 - b. Dorsal lingual branches of the lingual artery.
 - c. Ascending pharyngeal branch of the external carotid artery.
 - d. The greater palatine branch of the maxillary artery.

Venous drainage: Palatine, pharyngeal, or facial veins.

Lymphatic drainage: Jugulodigastric node.

Nerve supply: Glossopharyngeal and lesser palatine nerves.

5. PARANASAL SINUSES**Q. 1. Describe the paranasal sinuses.**

(TNMGR, April 2012)

Ans. Paranasal sinuses are air-filled spaces present within some bones around the nasal cavities. These are:

1. Frontal sinus
2. Maxillary sinus
3. Sphenoidal sinus
4. Ethmoidal sinus

All of them open into the nasal cavity through its lateral wall.

Function: To make the skull lighter and resonance to the voice. To provide resistance against trauma. To humidify the inhaled air.

Q. 2. Write short note on ethmoid air sinuses.

(TNMGR, Oct. 2000)

Ans. Ethmoidal sinuses are numerous small intercommunicating spaces which lie within the labyrinth of the ethmoid bone.

Subgroups

1. **Anterior ethmoidal sinus:** 1–11 air cells. It opens into the anterior part of the hiatus semilunaris of the nose. It is supplied by anterior ethmoidal nerve and vessels and drain into submandibular lymph nodes.
2. **Middle ethmoidal sinus:** 1–7 air cells. It opens into middle meatus of the nose. It is supplied by posterior ethmoidal vessels and nerve and orbital branches of pterygopalatine ganglion and drain into submandibular lymph nodes.
3. **Posterior ethmoidal sinus:** 1–7 air cells. It opens into superior meatus of the nose. It is supplied by posterior ethmoidal vessels and nerve and orbital branches of pterygopalatine ganglion and drain into the retropharyngeal lymph node.

Q. 3. Write a note on applied anatomy of maxillary air sinus.

(KUHS, July 2012)

Q. Discuss in detail about anatomy and applied importance of maxillary air sinuses.

(TNMGR, April 2000; BFUHS, Nov. 2002; KLE Uni. Jan. 2009)

Ans. The maxillary sinus is a large cavity in the body of maxilla. It is pyramidal in shape, with its base directed

medially towards the lateral wall of nose and the apex directed laterally into the zygomatic process of maxilla.

1. The sinus opens into the middle meatus of nose usually by two openings, one of which is closed by mucous membrane. The large bony *hiatus* of the sinus is reduced in the articulated skull by following bones:

- From above, by uncinat process of ethmoid and descending part of lacrimal bone.
- From below, by inferior nasal concha.
- From behind, by perpendicular plate of palatine bone.

2. Size

Height: 3.7 cm.

Width: 2.5 cm.

Anteroposterior depth: 3.7 cm.

3. Its roof is formed by the floor of orbit and is traversed by the infraorbital canal. The floor is formed by the alveolar process of maxilla and lies about 1.2 cm below the level of floor of nose.

Development: Maxillary sinus is first to develop. It appears as a shallow groove on the medial surface of maxilla during fourth month of intrauterine life, grows rapidly during 6 to 7 years, and reaches full size after the eruption of all permanent teeth.

Processes of Maxilla

1. **Zygomatic process:** The zygomatic process is a pyramidal lateral projection on which the anterior, posterior and superior surfaces of maxilla converge.

2. Frontal process

- Frontal process* articulates with the nasal margin of frontal bone, nasal bone, and lacrimal bone.
- Lateral surface* is divided by a vertical ridge, the *anterior lacrimal crest*, which gives attachment to lacrimal fascia and the medial palpebral ligament.
- Medial surface* forms a part of the lateral wall of nose. From above downwards, the surface presents following features:
 - Uppermost area articulates with ethmoid.
 - Ethmoidal crest.
 - Atrium of the middle meatus.
 - Conchal crest.
 - The inferior meatus of the nose with nasolacrimal groove.

3. Alveolar process

- The alveolar process bears sockets for the roots of upper teeth.
- Buccinator arises from the posterior part of its outer surface.

3. A rough ridge, the maxillary torus, is sometimes present on the inner surface opposite of the molar sockets.

4. Palatine process

- Palatine process is a thick horizontal plate projecting medially from the lowest part of the nasal surface.
- Inferior surface is concave, and the two palatine processes form anterior three-fourths of the bony palate.
- Superior surface is concave from side to side, and forms greater part of the floor of the nasal cavity.
- Medial border is raised superiorly into the nasal crest. Groove between the nasal crests of two maxillae receives lower border of vomer.
- Posterior border articulates with horizontal plate of palatine bone.
- Lateral border is continuous with the alveolar process.

Arterial supply: Facial, infraorbital and greater palatine arteries.

Venous supply: Facial vein, pterygoid plexus of veins.

Nerve supply: Infraorbital, anterior, middle, posterior superior alveolar nerves.

Lymphatics: Submandibular lymph nodes.

Applied Aspect

- Infection of the sinus is known as *sinusitis*, with headache, persistent thick purulent discharge from the nose. Diagnosis is assisted by transillumination and radiography.
- Maxillary sinus is most commonly involved in this. It may be infected from nose or caries tooth. Drainage of the sinus is difficult because its ostium lies at a higher level than its floor. So the sinus is drains artificially by antrum puncture and by Caldwell-Luc operation.
- Carcinoma of maxillary sinus** arises from the mucosal lining. Symptoms depend on the direction of growth:
 - Invasion of the orbit:* Proptosis, diplopia, facial pain, and numbness of the skin over maxilla.
 - Invasion of the floor:* Bulging and ulceration of the palate.
 - Forward growth:* Obliterates the canine fossa, swelling of the face.
 - Backward growth:* Severe pain in upper teeth.
 - Growth in medial direction:* Nasal obstruction, epistaxis, and epiphora.

- f. *Growth in lateral direction*: Swelling on face, and palpable mass in labio-gingival groove.
4. Frontal sinusitis can produce a brain abscess in the frontal lobe. A similar abscess may result from ethmoiditis.

6. CRANIAL NERVES

Q. 1. Enumerate the cranial nerves. Write a note on trigeminal nerve. (TNMGR, Oct. 2000, 2012)

Q. Describe the origin, course, branches and clinical implications of fifth cranial nerve.

(Pacific Uni., May 2011)

Ans. Cranial nerves: 12 pairs of cranial nerves.

1. Olfactory
2. Optic nerve
3. Oculomotor nerve
4. Trochlear nerve
5. Trigeminal nerve
6. Abducent nerve
7. Facial nerve
8. Vestibulocochlear nerve
9. Glossopharyngeal nerve
10. Vagus nerve
11. Accessory nerve
12. Hypoglossal nerve

Trigeminal nerve: Fifth cranial nerve is the largest cranial nerve. It is the nerve of first brachial arch. Branches of this nerve provide sensory fibers to the four parasympathetic ganglia associated with cranial outflow of parasympathetic nervous system. These are ciliary, pterygopalatine, otic and submandibular.

Ophthalmic, the first division carries sensory fibers from the structures derived from frontonasal process.

Maxillary, the second division conveys afferent fibers from structures derived from maxillary process.

Mandibular, the third mixed division carries sensory fibers derives from mandibular process.

Trigeminal nerve is attached to lateral aspect of pons. It has two nuclei:

1. **General somatic afferent column (sensory):** This column has three nuclei. These are:
 - **Spinal nucleus:** It takes pain and temperature sensations from most of the face area which relay here. The crossed fibers are called **trigeminal lemniscus** which goes to ventroposteromedial nucleus of thalamus for another relay, to finally terminate in lower part of post central gyrus.

- **Superior sensory nucleus:** Fibers carrying touch and pressure relay in this nucleus. Remaining path is same as of spinal nucleus.
- **Mesencephalic nucleus:** This nucleus extends from pons till the midbrain. It receives proprioceptive impulses from muscles of mastication, temporomandibular joint and teeth.

2. **Branchial efferent column (motor):** The nucleus of 5th nerve is situated at the level of upper pons. The fibers of the motor nucleus supply muscles derived from first branchial arch.

Course: It is attached to the ventral surface of pons by a large sensory root and small motor root. The motor root lies ventromedial to the sensory root. The two roots pass forward to trigeminal ganglion in middle cranial fossa.

Sensory components of 5th nerve: Sensation of pain, temperature, touch and pressure from skin of face, mucous membrane of nose, most of the tongue, paranasal air sinuses travel along axons. Their cell bodies lie in the 5th ganglion or semilunar ganglion or gasserian ganglion. It lies at apex of petrous temporal bone in a dural cave, the Meckel's cave. Peripheral processes of the ganglion cells forms the three nerves. The central processes of 5th ganglion form sensory root. Some fibers ascend and other descends. Ascending fibers end in superior sensory nucleus. Descending fibers end in the spinal nucleus of 5th nerve.

Pain and temperature reach spinal nucleus. **Touch and pressure** sensations go to superior sensory nucleus.

Ophthalmic nerve fibers end in the inferior part, **maxillary nerve** fibers end in the middle part and **mandibular nerve** fibers terminate in the upper part of spinal nucleus.

Proprioceptive fibers from muscles of mastication, extraocular muscles and facial muscles bypass 5th ganglion to reach unipolar cells of mesencephalic nucleus.

Axons of neurons of spinal nucleus, superior sensory nucleus and central processes of cells of mesencephalic nucleus cross to the opposite side and ascend as trigeminal lemniscus. The lemniscus ends in the ventral posteromedial nucleus of thalamus, where these fibers relay. The third neuron fibers end in area 3, 1 and 2 of cerebral cortex.

Motor component: The motor nucleus receives impulses from the right and left cerebral hemispheres, red nucleus and mesencephalic nucleus. Fibers of motor root supply four muscles of mastication and tensor veli palatini, tensor tympani, mylohyoid and anterior belly of digastric.

Trigeminal nerve comprises three branches, ophthalmic V1, maxillary V2 and mandibular V3.

A. Ophthalmic Nerve

It is sensory. Its branches are:

1. Frontal

- a. *Supratrochlear*: Upper eyelid, conjunctiva, lower part of forehead.
- b. *Supraorbital*: Frontal air sinus, upper eyelid, forehead, scalp till vertex.

2. Nasociliary

- a. *Posterior ethmoidal*: Sphenoidal air sinus, posterior ethmoidal air sinuses.
- b. *Long ciliary*: Sensory to eyeball.
- c. Nerve to ciliary ganglion.
- d. *Infratrochlear*: Both eyelids, side of nose, lacrimal sac.
- e. *Anterior ethmoidal*
 - i. Middle and anterior ethmoidal sinuses
 - ii. Medial internal nasal
 - iii. Lateral internal nasal
 - iv. External nasal—skin of ala of vestibule and tip of nose

3. *Lacrimal*: Lateral part of the upper eyelid; conveys secretomotor fibers from zygomatic nerve to the lacrimal gland.

B. Maxillary Nerve

1. *In middle cranial fossa*: Meningeal branch.
2. *In pterygopalatine fossa*
 - a. Ganglionic branches
 - b. *Zygomatic*
 - i. Zygomaticotemporal
 - ii. Zygomaticofacial
 - c. Posterior superior alveolar
3. *In infraorbital canal*
 - a. Middle superior alveolar
 - b. Anterior superior alveolar
4. *On face*: Infraorbital
 - a. Palpebral
 - b. Labial
 - c. Nasal

C. Mandibular Nerve (TNMGR, April, Oct. 2013; KUHS, June 2013)

1. Trunk

- a. Meningeal
- b. Nerve to medial pterygoid

- Tensor veli palatini
- Tensor tympani
- Medial pterygoid

2. Anterior division

- a. Deep temporal
- b. Lateral pterygoid
- c. Masseteric
- d. Buccal—skin of cheek

3. Posterior division

- a. *Auriculotemporal*
 - Auricular
 - Superficial temporal
 - Articular to temporomandibular joint
 - Secretomotor to parotid gland.
- b. *Lingual*: General sensations from anterior two-thirds of tongue.
- c. *Inferior alveolar*: Lower teeth and nerve to mylohyoid:
 - Mylohyoid
 - Anterior belly of digastric

Applied Clinical Anatomy

1. *Injury to ophthalmic nerve*: Loss of corneal blink reflex.
2. *Injury to maxillary nerve*: Loss of sneeze reflex.
3. *Injury to mandibular nerve*: Loss of jaw jerk reflex.
4. Due to the peculiar sensory distribution of the nerve, headache is a common symptom in common cold, boils, sinusitis, infections of teeth, meninges, glaucoma, etc.
5. **Trigeminal neuralgia**: Trigeminal neuralgia is defined as sudden, unilateral, severe, brief, stabbing, lacerating, recurring pain in the distribution of one or more branches of the 5th cranial nerve. Treatment includes medicinal; surgical (peripheral injections, peripheral neurectomy, cryotherapy and thermo-coagulation).

Q. 2. Write a short note on infraorbital nerve.

(TNMGR, April 1998)

Ans. It is the continuation of the maxillary nerve. It enters the orbit through the inferior orbital fissure. It then runs forwards on the floor of the orbit or the roof of the maxillary sinus, at first in the infraorbital groove and then in the infraorbital canal remaining outside the periosteum of the orbit. It emerges on the face through the infraorbital foramen and terminates by dividing into palpebral, nasal and labial branches. The nerve is accompanied by the infraorbital branch of the third part of the maxillary artery and the accompanying vein.

Branches

1. The **middle superior alveolar nerve** arises in the infraorbital groove, runs in the lateral wall of the maxillary sinus, and supplies the upper premolar teeth. It may be duplicated, or may be absent.
2. The **anterior superior alveolar nerve** arises in the infraorbital canal, and runs in a sinuous canal having a complicated course in the anterior wall of the maxillary sinus. It supplies the upper incisors and canine teeth, the maxillary sinus, and the antero-inferior part of the nasal cavity.
3. Terminal branches (**palpebral, nasal and labial**) supply, a large area of skin on the face. They also supply the mucous membrane of the upper lip and cheek.

Q. 3. Describe the nuclei of origin, course, relations, distribution and applied anatomy of mandibular nerve.

(TNMGR, March 2010; KUHS, June 2013; MAHE, April 2014)

Q. Write a short note on lingual nerve.

(RGUHS, Nov. 2011)

Q. Write a short note on inferior alveolar nerve.

(TNMGR, Oct. 1996, 1999, Nov. 2001, Oct. 2003, March 2008; RGUHS, April 2007; KUHS, Jan. 2014)

Ans. This is the largest of the three divisions of the trigeminal nerve. It has both sensory and motor fibers. It is the nerve of the first branchial arch and supplies all structures derived from the mandibular or first branchial arch. Otic and submandibular ganglia are associated with the nerve.

Course and relations: Mandibular nerve begins in the middle cranial fossa through a large sensory root and a small motor root. The **sensory root** arises from the lateral part of the trigeminal ganglion and leaves the cranial cavity through the foramen ovale. The **motor root** lies deep to the trigeminal ganglion and to the sensory root. It also passes through the foramen ovale to join the sensory root just below the foramen thus forming the main trunk. The main trunk lies in the infratemporal fossa, on the tensor veli palatini, deep to the lateral pterygoid. After a short-course, the main trunk divides into a small anterior trunk and a large posterior trunk.

Branches

From the main trunk

- a. Meningeal branch
- b. Nerve to the medial pterygoid

From the anterior trunk

- a. Buccal nerve (sensory)

- b. Masseteric and deep temporal nerves and nerve to the lateral pterygoid (motor)

From the posterior trunk

- a. Auriculotemporal nerve
- b. Lingual nerve
- c. Inferior alveolar nerves

Meningeal branch or nervus spinosus: Supplies the dura mater of the middle cranial fossa.

Nerve to medial pterygoid: Supplies the medial pterygoid from the deep surface. This nerve gives a motor root to the otic ganglion which does not relay and supplies the tensor palatini and the tensor tympanic muscles.

Buccal nerve: Supplies skin of cheek and mucous membrane related to the buccinators. It also supplies the labial aspect of gums of molar and premolar teeth.

Masseteric nerve: Deep surface of the masseter. It also supplies the temporomandibular joint.

Deep temporal nerves: These are two nerves, anterior and posterior, supplies the deep surface of the temporalis.

Nerve to lateral pterygoid: It enters the deep surface of the muscle.

Auriculotemporal nerve: It arises by two roots which runs backwards, encircle the middle meningeal artery and unite to form a single trunk. The auricular part of the nerve supplies the skin of the tragus; upper parts of the pinna, external acoustic meatus and the tympanic membrane. The temporal part supplies the skin of the temple. In addition, the auriculotemporal nerve also supplies the parotid gland and the temporomandibular joint.

Lingual nerve: Lingual nerve is one of the two terminal branches of the posterior division of the mandibular nerve. It is sensory to the anterior two-thirds of the tongue and to the floor of the mouth.

Course and relations: It begins 1 cm below the skull. It runs first between the tensor veli palatini and the lateral pterygoid and then between the lateral and medial pterygoids. About 2 cm below the skull, it is joined by the chorda tympani nerve. Emerging at the lower border of the lateral pterygoid, the nerve runs downwards and forwards between the ramus of the mandible and the medial pterygoid. Next it lies in direct contact within the mandible, medial to the third molar tooth between the origin of the superior constrictor and mylohyoid muscles. It soon leaves the gum and runs over the hyoglossus deep to the mylohyoid. Finally, it lies on the surface of the genioglossus deep to the mylohyoid. Here, it winds around the submandibular duct and divides into its terminal branches.

Inferior alveolar nerve (KUHS, Jan. 2014): It is the larger terminal branch of the posterior division of the mandibular nerve. It runs vertically downwards lateral to the medial pterygoid and to the sphenomandibular ligament. It enters the mandibular foramen and runs in the mandibular canal. It is accompanied by the inferior alveolar artery.

Branches

- Mylohyoid branch** contains all the motor fibers of the posterior division. It arises just before the inferior alveolar nerve enters the mandibular foramen. It pierces the sphenomandibular ligament with the mylohyoid artery, runs in the mylohyoid groove, and supplies the mylohyoid muscle and the anterior belly of digastric.
- While running in the mandibular canal the inferior alveolar nerve gives branches that supply the lower teeth and gums.
- Mental nerve** emerges at the mental foramen and supplies the skin of the chin, and the skin and mucous membrane of the lower lip. Its incisive branch supplies the labial aspect of gums of canine and incisor teeth.

Q. 4. Describe the intracranial, intrapetrous and extracranial course, branches and clinical importance of the facial nerve.

(RGUHS, April 2007; BFUHS, May 2008; TNMGR, Sept. 2009; KUHS, Dec. 2012; MUHS, April, Oct. 2013)

Ans. Facial nerve (7th) is the nerve of the second branchial arch.

Functional Components

- Special visceral or branchial efferent:** Muscles of facial expression and elevation of the hyoid bone.
- General visceral efferent or parasympathetic:** Secretomotor to the submandibular and sublingual salivary glands, the lacrimal glands, and glands of nose, palate and pharynx.
- General visceral afferent:** Afferent impulses from submandibular and sublingual salivary glands, lacrimal glands, and glands of nose, palate and pharynx.
- Special visceral afferent fibers:** Taste sensation from anterior two-thirds of the tongue except from vallate papillae and from palate.
- General somatic afferent fibers:** Innervate a part of the skin of the ear.

Nuclei: The fibers of the nerve are connected to four nuclei situated in the lower pons.

- Motor nucleus or branchiomotor.
- Superior salivatory nucleus or parasympathetic.
- Lacrimal nucleus is also parasympathetic.

- Nucleus of the tractus solitarius which is gustatory and also receives afferent fibers from the glands.

The motor nucleus lies deep in the reticular formation of the lower pons. The part of the nucleus that supplies muscles of the upper part of the face receives corticonuclear fibers from the motor cortex of both the right and left sides. In contrast, the part of the nucleus that supplies muscles of the lower part of the face receives corticonuclear fibers only from the opposite cerebral hemisphere.

Course and Relations

- Intracranial course:** The facial nerve is attached to the brainstem by two roots, motor and sensory. The sensory root is also called the **nervus intermedius**. The two roots of the facial nerve are attached to the lateral part of the lower border of the pons. The two roots run laterally and forwards with the eighth nerve to reach the internal acoustic meatus. In the meatus, the motor root lies in a groove on the eighth nerve, with the sensory root intervening. At the bottom of the meatus, the two roots fuse to form a single trunk, which lies in the petrous temporal bone. Within the canal, the course of the nerve can be divided into three parts by two bends:
 - The **first part** is directed laterally above the vestibule.
 - The **second part** runs backwards in relation to the medial wall of the middle ear, above the promontory.
 - The **third part** is directed vertically downwards behind the promontory. The facial nerve leaves the skull by passing through the stylomastoid foramen.
- Extracranial course:** The facial nerve crosses the lateral side of the base of the styloid process. It enters the posteromedial surface of the parotid gland, runs forward through the gland crossing the retro-mandibular vein and the external carotid artery. Behind the neck of mandible, it divides into its five terminal branches which emerge along the anterior border of the parotid gland.

Branches and Distribution

- Within the facial canal**
 - Greater petrosal nerve:** Gustatory and parasympathetic fibers.
 - Nerve to the stapedius:** Stapedius muscle.
 - Chorda tympani.
- At its exit from the stylomastoid foramen**
 - Posterior auricular
 - Digastric
 - Stylohyoid

c. **Terminal branches within the parotid gland**

- i. Temporal
- ii. Zygomatic
- iii. Buccal
- iv. Marginal mandibular
- v. Cervical

d. **Communicating branches with adjacent cranial and spinal nerves:** In paralysis of the muscle, an even normal sound appears too loud and is known as hyperacusis.

Chorda tympani: It carries:

- a. **Preganglionic secretomotor fibers** to the submandibular ganglion for supply of the submandibular and sublingual salivary glands.
- b. **Taste fibers** from the anterior two-thirds of the tongue except circumvallate papillae.

Posterior auricular nerve: It supplies:

- a. Auricularis posterior
- b. Occipitalis
- c. Intrinsic muscles on the back of auricle

Digastric branch: Posterior belly of the digastric.

Stylohyoid branch: It supplies stylohyoid muscle.

Temporal branches

- a. Auricularis anterior
- b. Auricularis superior
- c. Intrinsic muscles on the lateral side of the ear
- d. Frontalis
- e. Orbicularis oculi
- f. Corrugator supercilii

Zygomatic branches: Orbicularis oculi.

Buccal branches: Buccinators.

Marginal mandibular branch: Muscles of lower lip and chin.

Cervical branch: Platysma.

Clinical Applied Anatomy

1. **Injury to stapedius:** Hyperacusis.
2. **Injury to zygomatic:** Epiphora and prevents blinking.
3. **Injury to buccal branch:** Dribbling from the mouth.
4. **Injury to marginal mandibular:** Paralysis of depressors of lower lip.
5. **Bell's palsy:** Sudden paralysis of facial nerve at the stylomastoid foramen, results in asymmetry of corner of mouth, inability to close the eye, dis-

appearance of nasolabial fold and loss of wrinkling of the skin of forehead on the same side.

6. Lesion above the origin of chorda tympani nerve will show symptoms of Bell's palsy with loss of taste from anterior two-thirds of tongue except vallate papillae.
7. Lesion above the origin of nerve to stapedius will cause symptoms 5, 6 and further causes hyperacusis. Lesions 5, 6 and 7 are lower motor neuron type. Upper motor neuron paralysis will not affect the upper part of face. The upper part of the face has bilateral representation whereas lower half has only ipsilateral representation.

Q. 5. Write a note on glossopharyngeal nerve.

(RGUHS, Nov. 2011; TNMGR, April 2012)

Ans. It is the 9th cranial nerve.

Functional Components

- a. **Special visceral efferent fibers:** Arise in nucleus ambiguus and supply the stylopharyngeus muscle.
- b. **General visceral efferent fibers (preganglionic):** Arise in inferior salivary nucleus and travel to otic ganglion, from where the postganglionic fibers supply to the parotid.
- c. **General visceral afferent fibers:** They are peripheral processes of cells in the inferior ganglion of the nerve. They carry general sensations from pharynx, carotid body and carotid sinus to the ganglion. The central processes convey these sensations to the nucleus of the solitary tract.
- d. **Special visceral afferent fibers:** They are peripheral processes of cells in the inferior ganglion of the nerve. They carry sensations of taste from the posterior one-third of the tongue including circumvallate papillae to the ganglion. The central processes convey these sensations to the nucleus of the solitary tract.
- e. **General somatic afferent fibers:** They are peripheral processes of cells in the inferior ganglion of the nerve. They carry general sensations (pain, touch, temperature) from the posterior one-third of the tongue, tonsil, and pharynx. The central processes convey these sensations to the nucleus of the spinal tract of trigeminal nerve.

Course

Intracranial: The fiber arises at the level of medulla oblongata. It is attached at the base of the brain in the posterolateral sulcus, and then enters jugular foramen.

Extracranial: Superior ganglion (small) is a detached part of inferior ganglion. Inferior ganglion carries all the sensory fibers. It enters the pharynx through the interval between constrictor muscles.

Branches and Distributions

1. **Tympanic nerve:** Middle ear, auditory tube, mastoid antrum and air cells.
2. **Lesser petrosal nerve:** Secretomotor for parotid gland.
3. **Carotid branch:** Carotid sinus and carotid body.
4. **Pharyngeal branches:** Mucous membrane of pharynx.
5. **Muscular branches:** Stylopharyngeus.
6. **Tonsillar branches:** Tonsil, soft palate, palatoglossal arch.
7. **Lingual branches:** Taste and general sensations from posterior one-third of the tongue.

Clinical Applied Anatomy

1. Paralysis of nerve leads to loss of reflex contraction of muscle of pharynx, and loss of taste sensation.
2. Glossopharyngeal neuralgia.

Q. 6. Write a short note on hypoglossal nerve.

(TNMGR, April 1997, 2000; RGUHS, Nov. 2011)

Ans. It is the 12th cranial nerve. It supplies the muscles of the tongue.

Function Components/Nuclear Columns

1. **General somatic efferent column:** The fibers arise from the hypoglossal nucleus which lies in the medulla, in the floor of fourth ventricle deep to the hypoglossal triangle.
2. **General somatic afferent column:** The nucleus is spinal nucleus of V cranial nerve where proprioceptive fibers from tongue end.

Nucleus: The hypoglossal nucleus lies in the floor of fourth ventricle beneath the hypoglossal triangle. Connection of the nucleus with opposite pyramidal tract forms supranuclear pathway of the nerve. It is also connected to cerebellum, reticular formation of medulla, sensory nuclei of V nerve and the nucleus of tractus solitarius.

Course and Relations

1. In their intraneural course, the fibers pass forwards lateral to the medial lemniscus and pyramidal tract, and medial to the reticular formation and olivary nucleus.
2. The nerve is attached to the anterolateral sulcus of the medulla, between the pyramid and the olive, by 10 to 15 rootlets. The rootlets run laterally behind the vertebral artery, and join to form two bundles which pierce the dura mater separately. The nerve leaves the skull through the hypoglossal canal.

3. During extracranial course, nerve first lies deep to the internal jugular vein, but soon inclines laterally between the internal jugular vein and the internal carotid artery.
4. It then descends between the internal jugular vein and the internal carotid artery in front of the vagus, deep to the parotid gland, styloid process, posterior belly of digastric, stylohyoid and posterior auricular and occipital arteries.
5. At the lower border of the posterior belly of the digastric, it curves forwards, hooks round the lower sternocleidomastoid branch of the occipital artery, crosses the internal and external carotid arteries and the loop of the lingual artery and passes deep to the posterior belly of digastric again to enter the submandibular region.
6. The nerve then continues forwards on the hyoglossus and genioglossus, deep to the submandibular gland and the mylohyoid and enters the substance of the tongue to supply all its intrinsic muscles and most of its extrinsic muscles.

Branches and distribution: Branches supply the extrinsic and intrinsic muscles of the tongue. Only extrinsic muscle, palatoglossus is supplied by fibers of the cranial accessory nerve through vagus and pharyngeal plexus.

Branches of the hypoglossal nerve containing fibers of nerve C1: These fibers join the nerve at the base of the skull.

1. **The meningeal branch:** Bone and meninges in the anterior part of the posterior cranial fossa.
2. **The descending branch:** Continues as the descends hypoglossi or the upper root of the ansa cervicalis.
3. Branches are also given to the thyrohyoid and geniohyoid muscles.

Clinical Applied Anatomy

Injury to this nerve leads to paralysis of muscles of the tongue on the side of lesion. Infranuclear lesion leads to hemiatrophy. Supranuclear lesion produces paralysis without wasting.

Q. 7. Write a short note on pterygopalatine ganglion.

(TNMGR, April 1998; KUHS, Jan. 2014)

Ans. Pterygopalatine or sphenopalatine ganglion is the largest parasympathetic ganglion, suspended by two roots of maxillary nerve. Functionally, it is related to cranial nerve 7th. It is also called the **ganglion of hay fever** (Fig. 1.10).

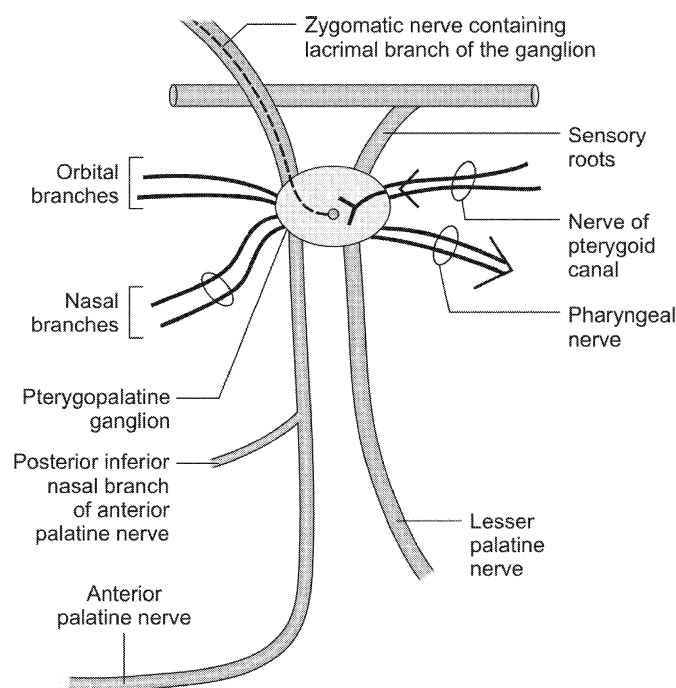


Fig. 1.10: Pterygopalatine ganglion and its relations

Roots

- **Sensory root** is from maxillary nerve. The ganglion is suspended by 2 roots of maxillary nerve.
- **Sympathetic root** is from postganglionic plexus around internal carotid artery. The nerve is called deep petrosal. It unites with greater petrosal to form **nerve of pterygoid canal**. The fibers of deep petrosal do not relay in the ganglion.
- **Secretomotor root** is from greater petrosal nerve arises from geniculate ganglion of cranial nerve 7th. These fibers relay in the ganglion.

Branches

1. **For lacrimal gland:** The postganglionic fibers pass through zygomatic branch of maxillary nerve. These fibers hitch-hike through zygomaticotemporal nerve into the communicating branch between zygomaticotemporal and lacrimal nerve, then to the lacrimal nerve for supplying the lacrimal gland.
2. **Nasopalatine nerve:** Secretomotor fibers to both nasal and palatal glands.
3. **Palatine branches:** Sensory and secretomotor fibers to mucous membrane and glands of soft palate and hard palate.
4. **Nasal branches:** Glands and mucous membrane of nasal septum.
5. **Orbital branches:** For the orbital periosteum.
6. **Pharyngeal branches:** For the glands of pharynx.

Q. 8. Write a short note on otic ganglion.

(RGUHS, Oct. 2010)

Ans. It is a periphery parasympathetic ganglion which relays secretomotor fibers to the parotid gland. Topographically, it is intimately related to the mandibular nerve, but functionally it is a part of the glossopharyngeal nerve. It is 2 to 3 cm in size, and is situated in the infratemporal fossa, just below the foramen ovale.

Connections and Branches

The **motor or parasympathetic root** is formed by the lesser petrosal nerve.

The **sympathetic root** is derived from the plexus on the middle meningeal artery. It contains postganglionic fibers arising in the superior cervical ganglion. The fibers pass through the otic ganglion without relay and reach the parotid gland via the auriculotemporal nerve. They are vasomotor in function.

The **sensory root** comes from the auriculotemporal nerve and is sensory to the parotid gland. Other fibers passing through the ganglion are as follows:

1. Nerve to medial pterygoid gives a motor root to the ganglion which passes through it without relay and supplies medially placed tensor tympani muscles.
2. Chorda tympani nerve is connected to the otic ganglion and also to the nerve of the pterygoid canal. These connections provide an alternative pathway of taste from the anterior two-thirds of the tongue.

Q. 9. Write a short note on submandibular ganglion.

(RGUHS, 2007)

Ans. This is a parasympathetic peripheral ganglion. It is a relay station for secretomotor fibers to the submandibular and sublingual salivary glands. Topographically, it is related to the lingual nerve, but functionally, it is connected to the chorda tympani branch of the facial nerve.

Connections and Branches

1. The **secretomotor fibers** pass from the lingual nerve to the ganglion through the posterior root. These are preganglionic fibers that arise in the superior salivatory nucleus and pass through nervus intermedius till the facial nerve, the chorda tympani and the lingual nerve to reach the ganglion or relay. **Postganglionic fibers** for the **submandibular gland** reach the gland through five or six branches from the ganglion.

Postganglionic fibers for the **sublingual** and **anterior lingual** glands re-enters the lingual nerve through the anterior root and travel to the gland through the distal part of the lingual nerve.

2. The **sympathetic fibers** are derived from the plexus around the facial artery. It contains postganglionic fibers arising in the superior cervical ganglion. They pass through submandibular ganglion without relay and supply vasomotor fibers to the submandibular and sublingual glands.
3. **Sensory fibers** reach the ganglion through the lingual nerve.

Q. 10. Write a short note on trigeminal ganglion.

(TNMGR, March 2008)

Ans. Trigeminal ganglion is the sensory ganglion of trigeminal nerve. The ganglion is crescentric or semi-lunar in shape. It lies in the trigeminal impression on the anterior surface of petrous temporal bone, in the trigeminal or Meckel's cave.

Relations

Medially: Internal carotid artery, posterior part of cavernous sinus.

Laterally: Middle meningeal artery.

Superiorly: Parahippocampal gyrus.

Inferiorly: Trigeminal nerve (motor root); greater petrosal nerve; petrous temporal bone (apex); foramen lacerum.

The central process of the ganglion cells forms the large sensory root of the trigeminal nerve. The peripheral processes of the ganglion cells form three divisions of the trigeminal nerve.

Blood supply: Internal carotid artery, middle meningeal, accessory meningeal arteries, and meningeal branch of ascending pharyngeal artery.

Q. 11. Write a short note on brachial plexus.

(TNMGR, April 2012)

Ans. The plexus consists of roots, trunks, divisions, cords and branches.

- a. **Roots:** These are constituted by the anterior primary rami of spinal nerves C5, 6, 7, 8 and T1 with contributions from the anterior primary rami of C4 and T2. The origin of the plexus may shift by one segment upward or downward, resulting in a pre-fixed or post-fixed plexus, respectively. In a pre-fixed plexus, the contribution by C4 is large and that from the T2 is often absent. In a post-fixed plexus, the contribution by T1 is large, T2 is always present, C4 is absent and C5 is reduced in size. The roots join to form trunks as follows.
- b. **Trunks:** Roots C5 and C6 join to form the **upper trunk**. Root C7 forms the **middle trunk**. Roots C8 and T1 join to form the **lower trunk**.

- c. **Divisions of the trunks:** Each trunk divides into ventral and dorsal divisions (which ultimately supply the anterior and posterior aspects of the limb). These divisions join to form cords.

d. **Cords**

- i. The lateral cord is formed by the union of ventral divisions of upper and middle trunks.
- ii. The medial cord is formed by the ventral division of the lower trunk.
- iii. The posterior cord is formed by union of the dorsal divisions of all the three trunks.

e. **Branches**

a. **Branches of the roots**

- i. Nerve to serratus anterior (C5, 6, 7)
- ii. Nerve to rhomboideus (C5)

b. **Branches of the trunks**

- i. Suprascapular nerve (C5, 6)
- ii. Nerve to subclavius (C5, 6)

c. **Branches of the cords**

1. **Branches of lateral cord**

- i. Lateral pectoral (C5–C7)
- ii. Musculocutaneous (C5–C7)
- iii. Lateral root of median (C5–C7)

2. **Branches of medial cord**

- i. Medial pectoral (C8, T1)
- ii. Medial cutaneous nerve of arm (C8, T1)
- iii. Medial cutaneous nerve of forearm (C8, T1)
- iv. Ulnar (C7, C8, T1)
- v. Medial root of median (C8, T1)

3. **Branches of posterior cord**

- i. Upper subscapular (C5, C6)
- ii. Nerve to latissimus dorsi (C6, C7, C8)
- iii. Lower subscapular (C5, C6)
- iv. Axillary (C5, C6)
- v. Radial (C5–C8, T1)

7. GLANDS: SALIVARY, THYROID AND PARATHYROID

Q. 1. Discuss the topographical anatomy of the parotid gland and its development. How is its secretory activity regulated?

(Bangalore Uni., Jan. 1992; Gujarat Uni., Oct. 2004; TNMGR, April 1997; March 2010; BFUHS, Oct. 2005; KUHS, July 2012; Pacific Uni., May 2015)

Ans. The parotid is the largest of the salivary glands. A part of this forward extension is often detached, and is known as the **accessory parotid** and it lies between the zygomatic arch and the parotid duct.

Capsule of parotid gland: The investing layer of the deep cervical fascia forms a capsule for the gland. The superficial lamina, thick and adherent to the gland, is attached above to the zygomatic arch. The deep lamina is thin and is attached to the styloid process, the mandible and tympanic plate. A portion of the deep lamina, extending between the styloid process and the mandible, is thickened to form the stylomandibular ligament which separates the parotid gland from the submandibular salivary gland.

External features: The gland resembles a three-sided pyramid. The apex of the pyramid is directed downwards. The gland has four surfaces:

1. Superior (base of the pyramid)
2. Superficial
3. Anteromedial
4. Posteromedial

The surfaces are separated by three borders:

1. Anterior
2. Posterior
3. Medial

Relations: The apex overlaps the posterior belly of the digastric and the adjoining part of carotid triangle. The cervical branch of the facial nerve and the two divisions of the retromandibular vein emerge through it.

surfaces: The **superior surface** or base forms the upper end of the gland which is small and concave. It is related to:

- a. Cartilaginous part of the external acoustic meatus.
- b. Posterior surface of the temporomandibular joint.
- c. Superficial temporal vessels.
- d. Auriculotemporal nerve.

The **superficial surface** is the largest of the four surfaces. It is covered with:

- a. Skin
- b. Superficial fascia
- c. Parotid fascia
- d. Deep parotid lymph nodes.

The **anteromedial surface** is grooved by the posterior border of the ramus of the mandible. It is related to:

- a. Masseter
- b. Lateral surface of the temporomandibular joint
- c. Posterior border of the ramus of the mandible
- d. Medial pterygoid
- e. Emerging branches of the facial nerve

The **posteromedial surface** is molded to the mastoid and the styloid processes and the structures attached to them. Thus, it is related to:

- a. Mastoid process, sternocleidomastoid and posterior belly of digastric.
- b. Styloid process with structures attached to it.

Borders (Fig. 1.11)

Anterior border separates the superficial surface from the anteromedial surface. The following structures emerge at the border:

- a. Parotid duct
- b. Terminal branches of the facial nerve
- c. Transverse facial vessels

Posterior border separates the superficial surface from the posteromedial surface. It overlaps the sternocleidomastoid.

Medial edge or border separates the anteromedial surface from the posteromedial surface. It is related to the lateral wall of the pharynx.

Structures within the parotid gland: From medial to the lateral side, these are as follows:

- i. **Arteries:** External carotid artery, maxillary artery, superficial temporal artery, transverse facial artery.
- ii. **Veins:** Retromandibular vein, superficial temporal and maxillary veins.
- iii. **Nerves:** Facial nerve and its terminal branches.
- iv. **Parotid lymph nodes.**

Parotid duct: It is thick-walled and is about 5 cm long. It emerges from the middle of the anterior border of the gland. It runs forwards and slightly downwards on the masseter. Its relations are:

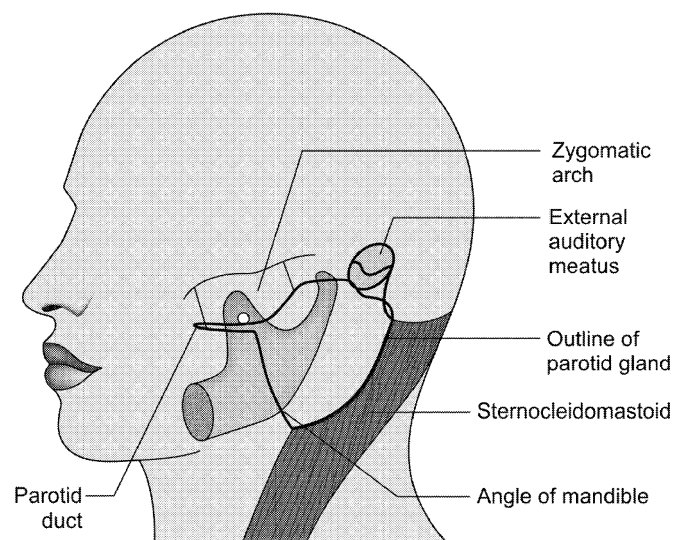


Fig. 1.11: Topography of parotid gland

Superiorly

- a. Accessory parotid gland
- b. Upper buccal branch of the facial nerve
- c. Transverse facial vessels.

Inferiorly: Lower buccal branch of the facial nerve. At the superior border of the masseter, it turns medially and pierces: buccal pad of fat, buccopharyngeal fascia, buccinators.

The duct runs forwards for a short distance between buccinator and the oral mucosa. Finally, the duct turns medially and opens into vestibule of the mouth opposite the crown of the upper second molar tooth.

Blood supply: External carotid artery and its branches. The veins drain into the external jugular vein.

Nerve supply

- a. **Parasympathetic nerves** are secretomotor. They reach the gland through the auriculotemporal nerve. **Preganglionic fibers** begin in the inferior salivatory nucleus; pass through the glossopharyngeal nerve, its tympanic branch, the tympanic plexus and the lesser petrosal nerve and relay in the otic ganglion. **Postganglionic fibers** pass through the auriculotemporal nerve and reach the gland.
- b. **Sympathetic nerves** are vasomotor and are derived from the plexus around the middle meningeal artery.
- c. **Sensory nerves** to the gland come from the auriculotemporal nerve, but the parotid fascia is innervated by the sensory fibers of the great auricular nerve (C2).

Lymphatics: Parotid nodes and upper deep cervical nodes.

Development: The parotid gland is ectodermal in origin. It develops from the buccal epithelium just lateral to the angle of mouth. The outgrowth branches repeatedly to form the duct system and acini. The mesoderm forms the intervening connective tissue septa.

Parotid lymph nodes: They drain:

- i. Temple
- ii. Side of the scalp
- iii. Lateral surface of the auricle
- iv. External acoustic meatus
- v. Middle ear
- vi. Parotid gland
- vii. Upper part of the cheek
- viii. Parts of the eyelids and orbit

Clinical Applied Anatomy

- i. **Parotid swellings** are very painful due to the unyielding nature of the parotid fascia.

- ii. **Mumps** is an infectious disease of the salivary glands caused by a specific virus. Viral parotitis or mumps characteristically does not suppurate. Its complications are orchitis and pancreatitis.
- iii. **Parotid abscess** is best drained by horizontal incision known as Hilton's method.
- iv. During surgical removal of the parotid gland or **parotidectomy**, the facial nerve is preserved by removing the gland in two parts, superficial and deep separately. The plane of cleavage is defined by tracing the nerve from behind forwards.
- v. **Mixed parotid tumor** is a slow growing lobulated painless tumor without any involvement of the facial nerve. Malignant change of such a tumor is indicated by pain, rapid growth, and fixity with hardness, involvement of the facial nerve, and enlargement of cervical lymph nodes.
- vi. **Parotid calculi** may get formed within the parotid gland or in its Stenson's duct. These can be located by injecting a radiopaque dye through its opening in the vestibule of the mouth. The procedure is called 'sialogram'. The duct can be examined by a spatula or bidigital examination.
- vii. **Parotidectomy** is the removal of the parotid gland. After this operation, at times, there may be regeneration of the secretomotor fibers in the auriculotemporal nerve which join the great auricular nerve. This causes stimulation of the sweat glands and hyperemia in the area of its distribution, thus producing redness and sweating in the area of the skin supplied by the nerve. This clinical entity is called **Frey syndrome**. Whenever such a person chews there is increased sweating in the region supplied by auriculotemporal nerve. So it is also called **auriculotemporal syndrome**. Areas supplied by this nerve are external auditory meatus, lateral surface of tympanic membrane and skin of temporal region.

Q. 2. Write about submandibular and sublingual salivary glands.

(Bangalore Uni., Jan. 1992; TNMGR, Oct. 2000)

Ans. Submandibular salivary gland: This is a large salivary gland, roughly J-shaped being indented by the posterior border of the mylohyoid which divides it into a larger part superficial to the muscle, and a small part lying deep to the muscle.

Superficial part: It has:

- a. Inferior
- b. Lateral
- c. Medial surface

The gland is partially enclosed between two layers of deep cervical fascia. The superficial layer of fascia covers the inferior surface of the gland and is attached to the base of the mandible. The deep layer covers the medial surface of the gland and is attached to the mylohyoid line of the mandible.

Relations: The inferior surface is covered by:

- Skin
- Platysma
- Cervical branch of the facial nerve
- Deep fascia
- Facial vein
- Submandibular lymph nodes

The lateral surface is related to:

- Submandibular fossa
- Medial pterygoid
- Facial artery.

The medial surface is related to:

- Mylohyoid muscle, nerve and vessels
- Hyoglossus
- Styloglossus muscles
- Lingual nerve
- Submandibular ganglion
- Hypoglossal nerve

Inferiorly, it overlaps stylohyoid and the posterior belly of digastrics.

Deep part: This part is small in size. It lies deep to the mylohyoid, and superficial to the hyoglossus and the styloglossus. Posteriorly, it is continuous with the superficial part round the posterior border of the mylohyoid. Anteriorly, it extends up to the posterior end of the sublingual gland.

Submandibular duct: It is thin-walled, and is about 5 cm long. It emerges at the anterior end of the deep part of the gland and runs forwards on the hyoglossus, between the lingual and hypoglossal nerves. At the anterior border of the hyoglossus, the duct is crossed by the lingual nerve. It opens on the floor of the mouth, on the summit of the sublingual papilla, at the side of the frenulum of the tongue.

Blood supply and lymphatic drainage: It is supplied by the facial artery. The veins drain into the common facial or lingual vein. Lymph passes to submandibular lymph nodes.

Nerve supply: It is supplied by branches from the submandibular ganglion. These branches convey:

- Secretomotor fibers
- Sensory fibers from the lingual nerve

- Vasomotor sympathetic fibers from the plexus on the facial artery.

Sublingual salivary glands: This is the smallest of the three salivary glands. It is almond-shaped and weighs about 3 to 4 g. It lies above the mylohyoid, below the mucosa of the floor of the mouth, medial to the sublingual fossa of the mandible and lateral to the genioglossus. About 15 ducts emerge from the gland. Most of them open directly into the floor of the mouth on the summit of the submental arteries. The nerve supply is similar to that of the submandibular gland.

Q. 3. Write about development of salivary glands.

(TNMGR, Sept. 2007)

Ans. The salivary glands develop as outgrowths of the buccal epithelium. The outgrowths are at first solid and are later canalized. They branch repeatedly to form the duct system. The terminal parts of the duct system develop into secretory acini. As the salivary glands develop near the junctional area between the ectoderm of the stomatodaeum and the endoderm of the foregut, it is difficult to determine whether they are ectodermal or endodermal. The outgrowth for the parotid gland arises in relation to the line along which the maxillary and mandibular processes fuse to form the cheek. It is generally considered to be ectodermal. The outgrowths for the submandibular and sublingual glands arise in relation to the linguogingival sulcus. They are usually considered to be of endodermal origin. One or more of the salivary glands may sometimes be absent.

Q. 4. Write a note on histology of salivary glands.

(KUHS, Jan. 2014)

Ans. Salivary glands are tubule-alveolar glands (racemose glands).

In the parotid gland, the cells of secretory element, the alveoli are made up of entirely serous cells (homocrine gland).

In the submandibular gland, the secretory cells are both serous and mucous (heterocrine gland).

In the sublingual gland, predominantly mucous secretory cells are present.

Q. 5. Write a short note on thyroid gland.

(TNMGR, March, 2002)

Ans. The gland consists of right and left lobes that are joined to each other by the isthmus. A third, pyramidal lobe, may project upwards from the isthmus (or from one of the lobes).

Situation and Extent

- The gland lies against vertebrae C5, C6, C7 and T1, embracing the upper part of the trachea.

2. Each lobe extends from the middle of thyroid cartilage to the fourth or fifth tracheal ring.
3. The isthmus extends from the second to the fourth tracheal ring.

Dimensions and weight: Each lobe measures about 5 cm × 2.5 cm × 2.5 cm, and the isthmus 1.2 cm × 1.2 cm. On an average, the gland weighs about 25 g.

Capsules of Thyroid

1. **True capsule:** Peripheral condensation of the connective tissue of the gland.
2. **False capsule:** It is derived from the pretracheal layer of the deep cervical fascia. It is thin along the posterior border of the lobes, but thick on the inner surface of the gland where it forms a suspensory (of Berry) ligament, which connects the lobe to the cricoid cartilage.

Relations: The lobes are conical in shape having:

- a. An apex
- b. A base
- c. *Three surfaces:* Lateral, medial and posterolateral.
- d. *Two borders:* Anterior and posterior.

Apex is directed upwards and slightly laterally. It is limited superiorly by the attachment of the sternothyroid to the oblique line of thyroid cartilage.

Base is on level with the 4th or 5th tracheal ring.

Lateral or superficial surface is convex, and is covered by:

- i. Sternohyoid.
- ii. Superior belly of the omohyoid.
- iii. Sternothyroid.
- iv. Anterior border of the sternocleidomastoid.

Medial surface is related to:

- i. *Two tubes:* Trachea and esophagus.
- ii. *Two muscles:* Inferior constrictor and cricothyroid.
- iii. *Two nerves:* External laryngeal and recurrent laryngeal.

Posterolateral or posterior surface is related to the carotid sheath and overlaps the common carotid artery.

Anterior border is thin and is related to the anterior branch of superior thyroid artery.

Posterior border is thick and rounded. It is related to:

- i. Inferior thyroid artery
- ii. Anastomoses between the superior and inferior thyroid arteries
- iii. Parathyroid glands
- iv. Thoracic duct

Isthmus has:

- i. Two surfaces, anterior and posterior
- ii. Two borders, superior and inferior

The anterior surface is covered by:

- i. The right and left sternothyroid and sternohyoid muscles
- ii. The anterior jugular veins
- iii. Fascia and skin

The posterior surface is related to the second to fourth tracheal rings. The upper border is related to the anastomosis between the right and left superior thyroid arteries. Lower border—inferior thyroid veins leave the gland at this border.

Arterial supply

1. Superior thyroid artery
2. Inferior thyroid artery
3. Lowest thyroid artery (**thyroidea ima artery**)
4. Accessory thyroid arteries arising from tracheal and esophageal arteries

Venous drainage: The thyroid is drained by the superior, middle and inferior thyroid veins.

Lymphatic drainage: Upper part: Upper deep cervical lymph nodes. Lower part: Lower deep cervical nodes directly.

Nerve supply: Middle cervical ganglion and superior and inferior cervical ganglia.

Histology: The gland is made up of two types of secretory cells:

- a. *Follicular cells:* During active phase—columnar, during resting phase—cuboidal.
- b. Parafollicular cells (C cells).

Development: From median endodermal thyroid diverticulum.

Clinical Applied Anatomy

1. Any swelling of the thyroid gland moves with deglutition.
2. Removal of thyroid with true capsule is necessary in thyrotoxicosis.
3. Hypothyroidism causes cretinism in infants and myxedema in adults.
4. Benign tumors may displace the neighboring structures.
5. Malignant tumors tend to invade the neighboring structures.

8. INTRACRANIAL VENOUS SINUSES

Q. 1. Name the venous sinuses of the cranium (dura mater). (TNMGR, Sept. 2008; BFUHS, May 2011)

Ans. These are venous spaces formed by dura mater.

Paired venous sinuses

1. Cavernous sinus
2. Superior petrosal sinus
3. Inferior petrosal sinus
4. Transverse sinus
5. Sigmoid sinus
6. Sphenoparietal sinus
7. Petrosquamous sinus
8. Middle meningeal sinus

Unpaired venous sinuses:

1. Superior sagittal sinus
2. Inferior sagittal sinus
3. Straight sinus
4. Occipital sinus
5. Anterior intercavernous sinus
6. Posterior intercavernous sinus
7. Basilar plexus of veins.

Q. 2. Write short note on relations and tributaries of the cavernous sinus. (TNMGR, April 2000)

Ans. A cavernous sinus is a large venous space situated in the middle cranial fossa, on either side of the body of the sphenoid bone.

Relations

Structures Outside the Sinus

- a. **Superiorly:** Optic tract, optic chiasma, olfactory tract, internal carotid artery, anterior perforated substance.
- b. **Inferiorly:** Foramen lacerum, junction of the body and greater wings of the sphenoid bone.
- c. **Medially:** Hypophysis cerebri, sphenoidal air sinus.
- d. **Laterally:** Temporal bone with uncus.
- e. **Anteriorly:** Superior orbital fissure, apex of the orbit.
- f. **Posteriorly:** Apex of the petrous temporal, crus cerebri of the midbrain.

Structures in the Lateral Wall of the Sinus (From Above Downward)

- a. Oculomotor nerve
- b. Trochlear nerve
- c. Ophthalmic nerve
- d. Maxillary nerve
- e. Trigeminal ganglion

Structures Passing through the Centre of the Sinus

- a. Internal carotid artery with venous and sympathetic plexus.
- b. Abducent nerve.

Tributaries (Incoming Channels)

From the orbit

- a. Superior ophthalmic vein
- b. Inferior ophthalmic vein
- c. Central vein of retina

From the brain

- a. Superficial middle cerebral vein
- b. Inferior cerebral veins

From the meninges

- a. Sphenoparietal sinus
- b. Frontal trunk of the middle meningeal vein

Distributaries (Draining Channels)

- a. **Transverse sinus:** Through superior petrosal sinus.
- b. **Internal jugular vein:** Through inferior petrosal sinus and plexus around internal carotid artery.
- c. **Pterygoid plexus of veins:** Through emissary veins.
- d. **Facial vein:** Through superior ophthalmic vein.
- e. Right and left cavernous sinuses communicate with each other through the anterior posterior intercavernous sinuses and basilar plexus of veins.

Clinical Applied Anatomy

1. **Thrombosis of cavernous sinus** may be caused by infection in dangerous area of face, nasal cavity and paranasal sinuses. Symptoms include: severe pain in the eye and forehead; paralysis of muscle supplied by 3, 4, 6 cranial nerves; marked edema of eyelid, cornea, and root of nose; exophthalmos.
2. **Pulsating exophthalmos:** Due to communication between cavernous sinus and internal carotid artery, due to head injury.

Q. 3. Write a short note on sagittal sinus.

(TNMGR, Oct. 2011)

Ans. a. Superior sagittal sinus: It occupies the upper convex attached margin of the falx cerebri. This sinus receives tributaries from:

1. Superior cerebral veins
2. Parietal emissary veins
3. Venous lacunae
4. A vein from nose

b. Inferior sagittal sinus: It is a small channel lies in the posterior two-thirds of the lower, concave, free margin of the falx cerebri. It ends by joining the great cerebral vein to form the straight sinus.

Clinical Applied Anatomy

Thrombosis of superior sagittal sinus may be caused by spread of infection from nose, scalp and diploe. This leads to:

1. Marked rise in intracranial tension due to defective absorption of CSF.
2. Delirium and convulsions due to congestion of superior cerebral veins.
3. Paraplegia of upper motor neuron type due to bilateral involvement of paracentral lobules of the cerebrum.

Q. 4. Write a note on falx cerebri.

(TNMGR, April 2001)

Ans. The falx cerebri is a large sickle-shaped fold of dura mater occupying the median longitudinal fissure between the two cerebral hemispheres. It has

a. Two ends

1. *Anterior end*: Narrow, attached to crista galli.
2. *Posterior end*: Broad, attached along the median plane to the upper surface of the tentorium cerebelli.

b. Two margins

1. *Upper margin*: Convex and is attached to the lips of the sagittal sulcus.
2. *Lower margin*: Concave and free.

c. Two surfaces

Right and left surfaces each of which is related to the medial surface of the corresponding cerebral hemisphere.

Three important venous sinuses are present in relation to this fold. The superior sagittal sinus lies along the upper margin; the inferior sagittal sinus along the lower margin and the straight sinus along the line of attachment of the falx to the tentorium cerebelli.

9. PHARYNX AND LARYNX

Q. 1. Write about muscles of larynx.

(TNMGR, Oct. 1999)

Ans. Intrinsic muscles of larynx: The attachments of intrinsic muscles of larynx are:

Nerve supply: All intrinsic muscles of the larynx are supplied by the recurrent laryngeal nerve **except** for the cricothyroid which is supplied by the external laryngeal nerve.

Actions

1. *Muscles which abduct the vocal cords*: Posterior cricoarytenoid.
2. *Muscles which adduct the vocal cords*: Lateral cricoarytenoid, transverse arytenoids, oblique arytenoids.
3. *Muscles which tense the vocal cords*: Cricothyroid.
4. *Muscles which relax the vocal cords*: Thyroarytenoid.
5. *Muscles which close the inlet of the larynx*: Aryepiglotticus.
6. *Muscles which open the inlet of larynx*: Thyroepiglottic (see table below).

10. TRIANGLES OF NECK: FACIAL SPACES AND LYMPH NODES

Q. 1. Write a note on digastric triangle.

(TNMGR, April 2001; Sept. 2010)

Ans. The area between the body of the mandible and the hyoid bone is known as the submandibular region. The superficial structures of this region lie in the submental and digastric triangles.

Boundaries

Anteroinferiorly: Anterior belly of digastric.

Posteroinferiorly: Posterior belly of digastric and stylohyoid.

Muscle	Origin	Fibers	Insertion
Cricothyroid	Lower border and lateral surface of cricoid.	It passes backwards and upwards.	Inferior cornua and lower border of thyroid cartilage.
Posterior cricoarytenoid	Posterior surface of the lamina of cricoid.	Upwards and laterally.	Posterior aspect of muscular process of arytenoids.
Lateral cricoarytenoid	Lateral part of upper border of arch of cricoid.	Upwards and backwards.	Anterior aspect of muscular process of arytenoid.
Transverse arytenoids	Posterior surface of one arytenoid.	Transverse.	Posterior surface of another arytenoid.
Oblique arytenoid and aryepiglotticus	Muscular process of one arytenoid.	Oblique.	Apex of the other arytenoid.
Thyroarytenoid and thyroepiglottic	Thyroid angle and adjacent cricothyroid ligament.	Backwards and upwards.	Anterolateral surface of arytenoid cartilage.

Superiorly or base: Base of the mandible and a line joining the angle of the mandible to the mastoid process.

Roof

1. Skin
2. *Superficial fascia, containing:*
 - a. Platysma
 - b. Cervical branch of the facial nerve
 - c. Ascending branch of the transverse or anterior cutaneous nerve of the neck
3. Deep fascia, which splits to enclose the submandibular salivary gland.

Floor: Mylohyoid muscle anteriorly and hyoglossus posteriorly.

Contents

Anterior part of the triangle

1. *Structures superficial to mylohyoid are*
 - a. Superficial part of the submandibular salivary gland
 - b. Submental artery
 - c. Mylohyoid nerve and vessels
2. *Structures superficial to the hyoglossus are*
 - a. Submandibular salivary gland
 - b. Intermediate tendon of the digastric and the stylohyoid
 - c. Hypoglossal nerve

Posterior part of the triangle

1. *Superficial structures*
 - a. Lower part of the parotid gland
 - b. External carotid artery
2. *Deep structures*
 - a. Styloglossus
 - b. Stylopharyngeus
 - c. Glossopharyngeal nerve
 - d. Pharyngeal branch of the vagus nerve
 - e. Styloid process
 - f. Part of the parotid gland
3. *Deepest structures*
 - a. Internal carotid artery
 - b. Internal jugular vein
 - c. Vagus nerve

The submandibular lymph nodes drain:

- a. Centre of the forehead.
- b. Nose with the frontal, maxillary and ethmoidal air sinuses.
- c. Inner canthus of the eye.

- d. Upper lip, anterior part of the cheek with the underlying gum and teeth.
 - e. Outer part of the lower lip with the lower gums and teeth excluding the incisors.
 - f. Anterior two-thirds of the tongue excluding the tip, and the floor of the mouth.
- The efferents from the submandibular nodes pass mostly to the jugulo-omohyoid node and partly to the jugulodigastric node.

Q. 2. Describe the carotid triangle of the neck.

(MUHS, April 2014)

Ans.

Boundaries

Anterosuperiorly: Posterior belly of the digastric muscle and the stylohyoid.

Anteroinferiorly: Superior belly of the omohyoid.

Posteriorly: Anterior border of the sternocleidomastoid muscle.

Roof

1. Skin
2. *Superficial fascia containing*
 - a. Platysma
 - b. Cervical branch of the facial nerve
 - c. Transverse cutaneous nerve of the neck
3. Investing layer of deep cervical fascia.

Floor: It is formed by parts of:

- a. Middle and inferior constrictors of the pharynx.
- b. Thyrohyoid muscle.
- c. Hyoglossus.

Contents

a. *Arteries*

- i. Common carotid artery
- ii. Internal carotid artery
- iii. External carotid artery—superior thyroid, lingual, facial, ascending pharyngeal and occipital branches.

b. *Veins*

- i. Internal jugular vein
- ii. Common facial vein
- iii. Pharyngeal vein
- iv. Lingual vein

c. *Nerves*

- i. Vagus
- ii. Superior laryngeal nerve
- iii. Spinal accessory nerve

- iv. Hypoglossal nerve
- v. Sympathetic chain
- d. Carotid sheath with its contents
- e. **Lymph nodes**
 - i. Deep cervical lymph nodes
 - ii. Jugulodigastric node
 - iii. Jugulo-omohyoid node.

Q. 3. Discuss the applied anatomy of various fascial spaces in relations to spread of infection from dental origin.

(TNMGR, March 2010; Sumandeep Vidyapeeth, April 2011)

Ans. The fascial spaces in head and neck are the potential spaces between the various layers of fascia normally filled with loose connective tissue and bounded by anatomical barriers, usually of bone, muscle or fascial layers.

Classification

Suprahyoid Spaces

1. Superficial facial compartment
2. Floor of the mouth:
 - a. Sublingual space
 - b. Submandibular space
 - c. Submental space
3. Masticator space:
 - a. Temporal space—(i) superficial, (ii) deep
 - b. Submasseteric space
 - c. Superficial pterygoid space
4. Parapharyngeal space including deep pterygoid space
5. Parotid compartment
6. Paratonsillar space
7. Space of the body of mandible.

Infrahyoid Spaces

1. Visceral compartment:
 - a. Pretracheal space/previsceral space
 - b. Retrovisceral space
2. Visceral space
3. Other spaces:
 - a. Cavity within carotid sheath
 - b. Space between 2 layers of prevertebral fascia.

A. Suprahyoid Spaces

1. Superficial Facial Compartment

Subdivisions

- i. **Canine space:** It overlies the canine fossa of maxilla and underneath levator labii superioris and levator labii superioris alaeque nasi.

- ii. **Buccal space:** It has following boundaries:

Laterally: Skin and subcutaneous tissue.

Medially: Buccinator and buccopharyngeal fascia.

Anteriorly: Labial musculature, posterior border of zygomaticus major, depressor anguli oris.

Posteriorly: Pterygo mandibular raphe and anterior edge of masseter muscle.

Superiorly: Zygomatic arch.

Inferiorly: Lower border of mandible.

Contents: Buccal pad of fat, parotid duct, facial artery.

Clinical implications: Canine space may be infrequently involved in odontogenic infections (roots of maxillary canine) and in nasal infections.

2. Floor of the Mouth

- i. **Sublingual spaces:** These are present above the mylohyoid muscle.

Boundaries

Laterally: Alveolar process of mandible above mylohyoid line.

Medially: Genioglossus and geniohyoid.

Roof: Mucosa.

Posteriorly: Body of hyoid bone, geniohyoid, genioglossus and styloglossus muscles.

Contents: Deep part of submandibular gland and submandibular duct, sublingual salivary gland, lingual vessels and nerve, hypoglossal nerve.

- ii. **Submental space:** It is a conical, small anterior, midline, single space.

Boundaries

Anterosuperiorly: Symphysis menti (apex of cone).

Posteroinferiorly: Hyoid bone (base of cone).

Superolaterally: Anterior belly of digastric.

Superficially: Skin, superficial fascia containing platysma, deep fascia.

Deep: Mylohyoid muscle.

Contents: Anterior jugular vein, submental lymph nodes.

Clinical significance: It may be involved in infections of mandibular incisors causing a swelling at the point of chin.

- iii. **Submandibular spaces:** These bilateral spaces are located lateral to submental space.

Boundaries

Superiorly: Mylohyoid, genioglossus.

Inferiorly: Skin, superficial fascia, platysma, deep fascia.

Laterally: Mandible.

Anteroinferiorly: Anterior belly of digastric.

Posteriorly: Posterior belly of digastric.

Contents: Submandibular salivary gland, submandibular lymph nodes, mylohyoid vessels and nerves.

Clinical implications: Submandibular space is perhaps the most commonly involved space in primary infections of head and neck. Infection may arise from injuries to the oral mucosa, submandibular or sublingual gland sialadenitis or infection from roots of mandibular teeth.

3. Masticator Space

Space formed by splitting of deep cervical fascia to include ramus of mandible, masseter, medial and lateral pterygoid and that part of temporalis muscle.

Subdivisions

- Temporal or zygomaticotemporal space:** It is a superior extension of the masticator space.
- Submasseteric space:** It is an inferior extension between lateral surface of ramus of mandible and deep surface of masseteric muscle.
- Superficial pterygoid or pterygomandibular space:** It is also an inferior extension between medial surface of ramus of mandible laterally, lateral surface of medial pterygoid muscle inferomedially and lateral pterygoid muscle superomedially.

Contents: Inferior alveolar nerve and vessels, lingual nerve, mandibular nerve, maxillary artery, loose connective tissue and fat.

Clinical significance: Masticator space may be infected from infection of zygoma, temporal bone or lower molar teeth. Infection of pterygomandibular space due to septic needles during the inferior dental nerve block anesthesia. Trauma to mandible involving molar teeth.

4. Parapharyngeal Space

It is also known as lateral pharyngeal space, peripharyngeal space, pharyngomasticator space, pharyngomaxillary space, or pterygopharyngeal space. Parapharyngeal space can be divided into:

- Lateral pharyngeal space:** This space is pyramidal in shape with apex directed inferiorly towards the lesser cornu of hyoid bone and base directed superiorly towards skull base.

Boundaries

Anteriorly: Posterior pharyngeal wall.

Posteriorly: Vertebrae with ligaments and muscles.

Laterally: Deep cervical fascia anteriorly and styloid process with its attached structures posteriorly and deep surface of parotid gland in between.

Medially: Midline fibrous septum.

Superiorly: Deep pterygoid space, base of skull.

Inferiorly: Hyoid bone.

Divisions and contents: This space is subdivided by styloid process into anterior and posterior compartments. Anterior compartment (called pre-styloid compartment) contains lymph nodes, ascending pharyngeal and facial arteries, maxillary artery, inferior alveolar nerve, lingual nerve, auriculotemporal nerve and loose areolar tissue. Posterior compartment (called post-styloid compartment) contains carotid sheath with its contents, 9, 11, 12th cranial nerves and cervical sympathetic chain.

Clinical significance: It may receive infection from teeth, submandibular gland, masticator space, parotid space and paratonsillar space. From this space infection can pass to retropharyngeal space and then to superior mediastinum.

ii. Retropharyngeal space

Boundaries

Anteriorly: Posterior wall of pharynx.

Posteriorly: Pre-vertebral fascia.

Superiorly: Base of skull.

Inferiorly: Communicates with superior mediastinum.

Clinical significance: It acts as a route through which infection from the mouth and throat can reach the superior mediastinum.

5. Parotid Compartment

The parotid gland is completely enclosed in a well-defined compartment of deep fascia derived from superficial layer of deep cervical fascia.

Contents: Parotid gland and parotid lymph nodes.

Clinical significance: Infection in this space may be because of infection of gland or lymph nodes and not a cellulitis in loose connective tissue. This infection may readily pass deep to parapharyngeal space.

6. Paratonsillar Space

This space contains palatine tonsils.

Boundaries

Laterally: Superior pharyngeal constrictor.

Medially: Mucous membrane of anterior and posterior pillar of fauces.

Superiorly: Extends into soft palate.

7. Space of the Body of the Mandible

This space to be formed by attachment of superficial layer of deep cervical fascia to both outer and inner surfaces of the body of mandible.

Boundaries

Anteriorly: Anterior belly of digastric.

Posteriorly: Pterygoids.

Inferiorly: Fascial layers.

Superiorly: Mandible.

Clinical significance: Infection of this space can occur from osteomyelitis secondary to dental infections. Infection may spread by rupture of its wall into the masticator space posteriorly or submandibular space inferiorly.

B. Infrahyoid Fascial Spaces

1. Visceral Compartment

The area of loose connective tissue surrounding the thyroid gland, trachea and esophagus as a whole was long known as visceral compartment.

a. Pre-tracheal space

Boundaries

Superiorly: Strap muscles and their fascia.

Inferiorly: Superior mediastinum.

Laterally: Root of the neck.

Clinical importance: This space can get infected from retrovisceral space, around the sides of esophagus and thyroid gland between the levels of upper border of thyroid cartilage and inferior thyroid artery; or directly by anterior perforation of esophagus.

b. Retrovisceral space

Boundaries

Superiorly: Base of skull.

Inferiorly: Superior mediastinum.

Clinical importance: This space may be infected by posterior perforation of esophagus or infection of deep cervical lymph nodes.

2. Visceral Space

The esophagus is enclosed in a connective tissue sheath continuous above with buccopharyngeal fascia, posterior surface of pharynx and adjacent to surface of thyroid gland and trachea. The visceral space is a potential space which may be imagined to exist between visceral fascia and the organs themselves (may these be trachea or esophagus). Actually, this visceral fascia is firmly united to structures which it covers and

the visceral space in the latter sense does not really exist. Also infections lying deep to the fascia on esophagus do not tend to spread within this fascia up and down the esophagus but rather perforate it to reach the visceral compartment.

Q. 4. Describe in detail about the structure of lymph node. Add a note on levels of lymph node.

(TNMGR, Sept. 2010)

Ans. Each cervical lymph node has cortical and medullary regions, and is covered by a fibrous capsule. The cortex consists of lymphocytes which are densely packed together to form spherical lymphoid follicles, whereas the medulla is composed of medullary trabeculae, medullary cords and medullary sinuses.

The para-cortex is an intermediate area between the cortex and the medulla, where the lymphocytes return to the lymphatic system from the blood circulation. In the medulla of the lymph node, the medullary trabeculae, composed of dense connective tissue similar to the capsule, act as a framework extending from the capsule and guides blood vessels and nerves to different regions of the lymph node. The medullary cords and medullary sinuses are composed of reticulum cells. The medullary cords contain mainly plasma cells and small lymphocytes, whilst the medullary sinuses are filled with lymph and are part of the sinus system of the lymph node.

Cervical lymph nodes contain blood vessels. The main artery enters the lymph node at the hilus, which then branches into arterioles. Some of the arterioles supply the capillary bed in the medulla and some of them run along the medullary trabeculae to the cortex where the arterioles further branch into capillaries and supply the lymphoid follicles. The rest of the arterioles run along the trabeculae and reach the capsule where they anastomose with other branches.

The venous system has a similar route as the arterial system. The venules converge to form small veins in the cortex. The small veins run along the trabeculae of the lymph node and reach the medulla where they further converge to form the main vein. The main vein leaves the lymph node at the hilus (Fig. 1.12).

Classification of Lymph Nodes

There are about 800 lymph nodes in the body and about 300 lymph nodes are located in the neck. The American Joint Committee on Cancer (AJCC) divides palpable cervical lymph nodes into seven levels which are based on the extent and level of cervical nodal involvement by metastatic tumor.

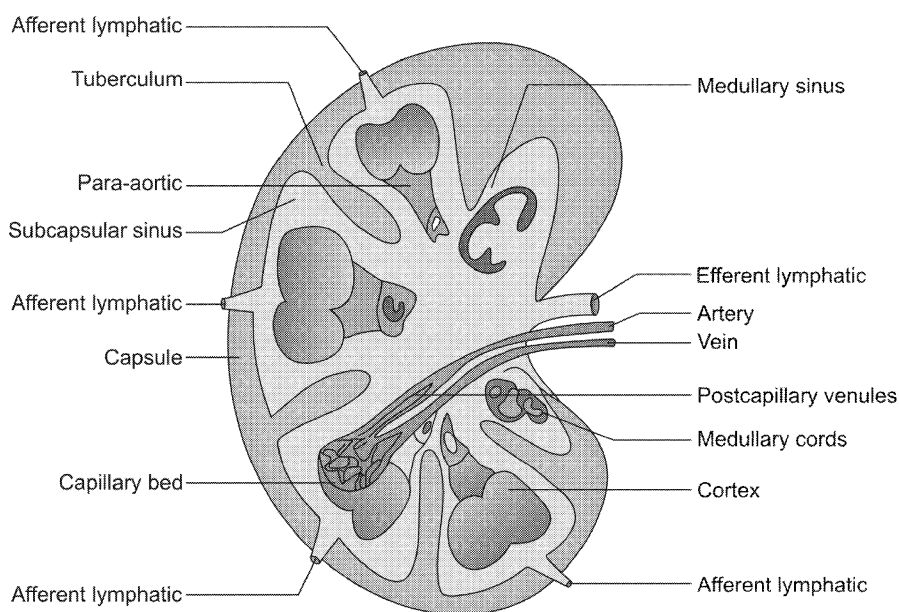


Fig. 1.12: Structure of lymph node

Level I: It contains the submental and submandibular triangles bounded by the posterior belly of digastric muscle, the hyoid bone inferiorly and the body of the mandible superiorly.

Level II: It contains the upper jugular lymph nodes and extends from the level of the skull base superiorly to the hyoid bone inferiorly.

Level III: It contains the middle jugular lymph nodes from the hyoid bone superiorly to the cricothyroid membrane inferiorly.

Level IV: It contains the lower jugular lymph nodes from the cricothyroid membrane superiorly to the clavicle inferiorly.

Level V: It contains the lymph nodes in the posterior triangle bounded by the anterior border of the sternocleidomastoid muscle anteriorly and the clavicle inferiorly. For descriptive purposes, level V may be further subdivided into upper, middle, and lower levels corresponding to the superior and inferior planes that define levels II, III, and IV.

Level VI: It contains the lymph nodes of the anterior compartment from the hyoid bone superiorly to the suprasternal notch inferiorly. They lie between the medial borders of the carotid sheaths.

Level VII: It contains the lymph nodes inferior to the suprasternal notch in the upper mediastinum.

Retropharyngeal, parotid, facial, occipital, and other nodes are referred to by these names.

Q. 5. Write a note on cervical chain of lymph nodes.
(RGUHS, 2006; Pacific Uni., May 2015)

Q. Classify lymph nodes and describe the lymphatic drainage of head and neck.

(TNMGR, March 2009; KLE Uni., Jan. 2009; MUHS, May 2010)

Ans. The entire lymph from the head and neck drains ultimately into the deep cervical nodes.

a. **Deep cervical nodes** form a vertical chain situated along the entire length of the internal jugular vein.

1. **Jugulodigastric node:** It lies below the posterior belly of digastric, between the angle of the mandible and anterior border of the sternocleidomastoid. It is the main node draining the tonsil.
2. **Jugulo-omohyoid node:** It lies just above the intermediate tendon of the omohyoid, under cover of the posterior border of the sternocleidomastoid. It is the main lymph node of the tongue.

Efferents of the deep cervical lymph nodes join together to form the jugular lymph trunks, one on each side. The left jugular trunk opens into the thoracic duct. The right trunk may open either into the right lymphatic duct, or directly into the angle of junction between the internal jugular and subclavian veins.

- b. **Peripheral nodes** are arranged in two circles:
- i. **Superficial circle** is made up of the following groups:
 1. Submental.
 2. Submandibular.

3. Buccal and mandibular (facial).
4. Preauricular (parotid).
5. Postauricular (mastoid).
6. Occipital.
7. Anterior cervical.
8. Superficial cervical nodes.

ii. **Deep circle (inner)** includes the following:

1. Prelaryngeal.
2. Pretracheal.
3. Paratracheal.
4. Retropharyngeal nodes.
5. Waldeyer's ring.

i. **Superficial Circle (Fig. 1.13)**

- a. **Submental nodes:** These drain the lymph from tip of the tongue and anterior part of floor of the mouth.
- b. **Submandibular nodes:** Drain lateral surface of tongue, lower gum and teeth and central area of forehead.
- c. **Buccal and mandibular nodes:** They drain part of the cheek and the lower eyelid.
- d. **Preauricular nodes:** Drain parotid gland, temporal region, middle ear, etc.
- e. **Postauricular (mastoid) nodes:** They drain a strip of scalp just above and behind the auricle, the upper half of the medial surface and margin of the auricle, and the posterior wall of the external acoustic meatus.
- f. **Occipital nodes:** They drain the occipital region of the scalp.

- g. **Anterior cervical nodes:** They drain the skin of the anterior part of the neck below the hyoid bone.
- h. **Superficial cervical nodes:** They drain the lobule of the auricle, the floor of the external acoustic meatus, and the skin over the lower parotid region and the angle of the jaw.

ii. **Deep Circle**

- a. **Prelaryngeal and pretracheal nodes:** They drain the larynx, the trachea and the isthmus of the thyroid.
- b. **Paratracheal nodes:** They receive lymph from the esophagus, the trachea and the larynx, and pass it onto the deep cervical nodes.
- c. **Retropharyngeal nodes:** They drain the pharynx, the auditory tube, the soft palate, the posterior part of the hard palate, and the nose. Their efferents pass to the upper deep cervical nodes.

Waldeyer's ring comprises lingual, palatine, tubal and nasopharyngeal tonsils.

Q. 6. Write a note on thoracic duct.

(TNMGR, April 2003; KUHS, July 2012)

Ans. The thoracic duct is the largest lymph trunk of the body. It begins in the abdomen from the upper end of the cisterna chyli, traverses the thorax, and ends on the left side of the root of the neck by opening into the angle of junction between the left internal jugular vein and the left subclavian vein. Before its termination, it forms an arch at the level of the transverse process of vertebra C7 rising 3 to 4 cm above the clavicle. The relations of the arch are given below:

Anterior

1. Left common carotid artery
2. Vagus
3. Internal jugular vein

Posterior

1. Vertebral artery and vein
2. Sympathetic trunk
3. Thyrocervical trunk or its branches
4. Prevertebral fascia
5. Phrenic nerve
6. Scalenus anterior

Apart from its tributaries in the abdomen and thorax, the thoracic duct receives:

1. The left jugular trunk
2. The left subclavian trunk
3. The left bronchomediastinal trunk

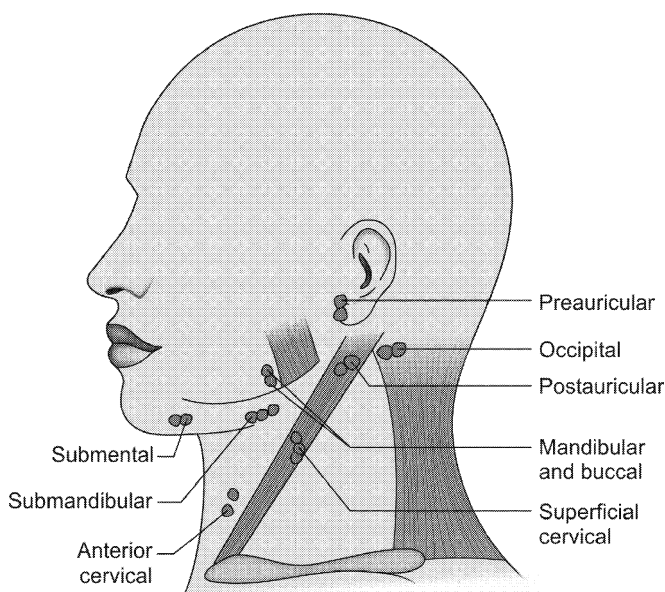


Fig. 1.13: Superficial lymph nodes of the neck

It drains most of the body, **except** for the right upper limb, the right halves of the head, the neck and the thorax and the superior surface of the liver. The **right jugular trunk** drains half of the head and neck. The **right subclavian trunk** drains the upper limb. The **bronchomediastinal trunk** drains the lung, half of the mediastinum and parts of the anterior walls of the thorax and abdomen. On the right side, the subclavian and jugular trunks may unite to form the **right lymph trunk** which ends in a manner similar to the thoracic duct.

Q. 7. Describe the deep cervical fascia.

(KUHS, Jan. 2014)

Ans. The deep fascia of the neck is condensed to form the following layers:

1. **Investing layer:** It lies deep to the platysma and surrounds the neck like a collar. It forms the roof of the posterior triangle of neck. It splits to enclose **muscles** (trapezius, sternocleidomastoid), **salivary glands** (parotid and submandibular), and **spaces** (suprasternal, supraclavicular).
2. **Pretracheal fascia:** This fascia encloses and suspends the thyroid gland and forms its false capsule. The posterior layer of thyroid capsule forms a thick suspensory ligament for thyroid, known as **ligament of Berry**. The fascia provides a slippery surface for the free movements of trachea during swallowing.
3. **Prevertebral fascia:** It lies in front of the prevertebral muscles and forms the floor of the posterior triangle of the neck. The cervical and brachial plexuses lie behind the prevertebral fascia. The fascia is pierced by cutaneous branches of the cervical plexus. This fascia provides a fixed base for the movements of the pharynx, esophagus and the carotid sheath during swallowing.
4. **Carotid sheath:** It is the condensation of the fibroareolar tissue around the main vessels of the neck. There are common and internal carotid arteries, internal jugular vein and vagus nerve.
5. **Buccopharyngeal fascia:** This fascia covers the superior constrictor muscle externally and extends onto the superficial aspect of the buccinator muscle.
6. **Pharyngobasilar fascia:** This fascia is especially thickened between the upper border of the superior constrictor muscle and the base of the skull. It lies deep to the pharyngeal muscles.

11. NASAL CAVITY AND ORBITS

Q. 1. Discuss the surgical anatomy of nose in detail.
(BFUHS, May 2011; MUHS, April 2011, 2013)

Q. Write in detail about the lateral wall of the nasal cavity.
(TNMGR, March 2008)

Ans.

a. **Nasal septum:** It is median osseocartilaginous partition between two halves of nasal cavity.

Bony part: Vomer, perpendicular plate of ethmoid.

Cartilaginous part: Septal cartilage, inferior nasal cartilage.

Cuticular part: Fibrofatty tissue covered by skin.

Arterial supply

1. **Anterosuperior part:** Anterior ethmoidal artery.
2. **Posteroinferior part:** Sphenopalatine artery.
3. **Anteroinferior part (little's area):** Superior labial artery.
4. **Posterosuperior part:** Posterior ethmoidal artery.

Venous drainage: Pterygoid venous plexus.

Nerve supply: General sensory nerves

- a. **Anterosuperior part:** Internal nasal branch.
- b. **Posteroinferior part:** Nasopalatine branch.
- c. **Posterosuperior part:** Medial posterior superior nasal branch.

Lymphatics: Submandibular, retropharyngeal and deep cervical lymph nodes.

b. **Lateral wall of nose:** It is irregular due to the presence of three shelf-like bony projections called conchae. The conchae increase the surface area of the nose for effective air-conditioning of the inspired air.

The lateral wall separates the nose:

- a. From the orbit above, with the ethmoidal air sinuses intervening.
- b. From the maxillary sinus below.
- c. From the lacrimal groove and nasolacrimal canal in front.

The lateral wall can be subdivided into three parts:

- a. A small depressed area in the anterior part is called the **vestibule**. It is lined by modified skin containing short, stiff, curved hairs called **vibrissae**.
- b. The middle part is known as the **atrium** of the middle meatus.

- c. The posterior part contains the conchae. Spaces separating the conchae are called **meatuses**.

The skeleton of the lateral wall is partly bony, partly cartilaginous, and partly made up only of soft tissues as follows:

The bony part is formed from before backwards by the following bones:

1. Nasal
2. Frontal process of maxilla
3. Lacrimal
4. Labyrinth of ethmoid with superior and middle conchae
5. Inferior nasal concha
6. Perpendicular plate of palatine bone together with its orbital and sphenoidal processes.
7. Medial pterygoid plate

The cartilaginous part is formed by:

- a. The superior nasal cartilage.
- b. The inferior nasal cartilage.
- c. 3 or 4 small cartilages of the ala.

The cuticular lower part is formed by fibrofatty tissue covered with skin.

Arterial supply

1. *Anterosuperior quadrant*: Anterior ethmoidal artery, posterior ethmoidal and facial arteries.
2. *Anteroinferior quadrant*: Facial and greater palatine arteries.
3. *Posterosuperior quadrant*: Sphenopalatine artery.
4. *Posteroinferior quadrant*: Greater palatine artery.

Venous drainage: Facial vein, pharyngeal plexus of veins, pterygoid plexus of veins.

Nerve supply

1. *General sensory nerves*
 - a. Anterosuperior quadrant: Anterior ethmoidal nerve.
 - b. Anteroinferior quadrant: Anterior superior alveolar nerve.
 - c. Posterosuperior quadrant: Posterior superior lateral nasal branches.
 - d. Posteroinferior quadrant: Anterior or greater palatine branch.
2. Special sensory nerves or olfactory nerves are distributed to the upper part of the lateral wall just below the cribriform plate of the ethmoid up to the superior concha.

Lymphatic drainage

1. *Anterior half*: Submandibular nodes.
2. *Posterior half*: Retropharyngeal and upper deep cervical nodes.

Q. 2. Write in detail about content of orbit and ocular muscles. (KUHS, Jan. 2014)

Ans. Each orbit resembles a four-sided pyramid on one side. The long axis of the orbit passes backwards and medially. The medial walls of the two orbits are parallel and the lateral walls are set at right angles to each other.

Roof: It is concave from side to side. It is formed—orbital plate of the frontal bone, and lesser wing of the sphenoid.

Relations

- a. It separates the orbit from the anterior cranial fossa.
- b. The frontal air sinus may extend into its anteromedial part.

Lateral wall: This is the thickest and strongest of all the walls of the orbit. It is formed by: Greater wing of the sphenoid bone and frontal process of the zygomatic bone.

Relations

- a. The greater wing of sphenoid separates the orbit from the middle cranial fossa.
- b. The zygomatic bone separates it from the temporal fossa.

Floor: It slopes upwards and medially to join the medial wall. It is formed by: Orbital surface of the maxilla, orbital surface of the zygomatic bone, orbital process of the palatine bone.

Relation: It separates the orbit from the maxillary sinus.

Medial wall: It is very thin. It is formed by: Frontal process of maxilla, lacrimal bone, orbital plate of the ethmoid, body of the sphenoid bone.

Relations

- a. The lacrimal groove, formed by the maxilla and the lacrimal bone, separates the orbit from the nasal cavity.
- b. The orbital plate of the ethmoid separates the orbit from the ethmoidal air sinuses.
- c. The sphenoidal sinuses are separated from the orbit only by a thin layer of bone.

Foramina in Relation to the Orbit

- i. The inferior orbital fissure transmits the zygomatic nerve, the orbital branches of the pterygopalatine ganglion, the infraorbital nerve and vessels, and the communication between the inferior ophthalmic vein and the pterygoid plexus of veins.

- ii. The infraorbital groove and canal transmit the corresponding nerve and vessels.
- iii. The zygomatic foramen transmits the zygomatic nerve.
- iv. The anterior ethmoidal foramina transmit the corresponding nerves and vessels. Posterior ethmoidal foramina only transmit vessels.

A. Content of Orbit

- 1. Eyeball.
- 2. *Fascia*: Orbital and bulbar.
- 3. *Muscles*: Extraocular.
- 4. *Vessels*: Ophthalmic artery, superior and inferior ophthalmic veins and lymphatics.
- 5. *Nerves*: Optic, oculomotor, trochlear, abducent, branches of ophthalmic and maxillary nerves and sympathetic nerves.
- 6. Lacrimal gland.
- 7. Orbital fat.

B. Muscles of Eye

I. Extraocular Muscles

a. Voluntary muscles

- 1. *Four recti*
 - i. Superior rectus
 - ii. Medial rectus
 - iii. Inferior rectus
 - iv. Lateral rectus
- 2. *Two obliqui*
 - i. Superior oblique
 - ii. Inferior oblique
- 3. The levator palpebrae superioris elevates the upper eyelid.

b. Involuntary muscles

- 1. *Superior tarsal muscle*: It elevates the upper eyelid.
- 2. *Inferior tarsal muscle*: It depresses the lower eyelid.
- 3. *Orbitalis*: Its action is uncertain.

Nerve Supply

- 1. *Superior oblique*: Trochlear nerve (SO_4).
- 2. *Lateral rectus*: Abducent nerve (LR_6).
- 3. *Remaining extraocular muscles and part of levator palpebrae superioris*: Oculomotor nerve.

Actions

- 1. Medial and lateral recti adduct and abduct the cornea, respectively.
- 2. Superior and inferior recti cause simple elevation and depression, respectively.

- 3. *Upward rotation or elevation*: Superior rectus and the inferior oblique.
- 4. *Downward rotation or depression*: Inferior rectus and the superior oblique.
- 5. *Medial rotation or adduction*: Medial rectus, the superior rectus and the inferior rectus.
- 6. *Lateral rotation or abduction*: Lateral rectus, the superior oblique and the inferior oblique.
- 7. *Intortion*: Superior oblique and the superior rectus.
- 8. *Extortion*: Inferior oblique and the inferior rectus.

12. STRUCTURE AND FUNCTION OF BRAIN.

Q. 1. Write a short note on taste pathways.

(TNMGR, March 2002)

Ans.

- 1. The taste from **anterior two-thirds** of tongue **except** from vallate papillae is carried by chorda tympani branch of facial nerve till the geniculate ganglion. The central processes go to the tractus solitarius in the medulla.
- 2. Taste from **posterior one-third** of tongue including the vallate papillae is carried by cranial nerve 9th till the inferior ganglion. The central processes also reach the tractus solitarius.
- 3. Taste from **posteriormost** part of tongue and epiglottis travels through vagus nerve till the inferior ganglion of vagus. These central processes also reach tractus solitarius.
- 4. After a relay in tractus solitarius, the solitario-thalamic tract is formed which becomes a part of trigeminal lemniscus and reaches postero-ventromedial nucleus of thalamus of the opposite side. Another relay here takes them to lowest part of postcentral gyrus, which is the area for taste.

Q. 2. Write a short note on motor speech area.

(TNMGR, Sept. 2002)

Ans. Primary motor area: It is located in the precentral gyrus, and in the anterior part of paracentral lobule on the medial surface of cerebral hemispheres. This corresponds to area 4 of Brodmann. Electrical stimulation of primary motor areas elicits contraction of muscles that are mainly on the opposite side of the body. Although cortical control of musculature is mainly contralateral, there is significant ipsilateral control of most of the muscles of the head and axial muscles of the body. The contralateral half of the body is represented as upside down, except the face. The pharyngeal region, tongue is represented in the most ventral and lower part of precentral gyrus, followed by the face, hand, arm, trunk and thigh. The remainder

of leg, foot and perineum is on the medial surface of hemisphere in the paracentral lobule.

Premotor area: This area coincides with the Brodmann's area 6 and is situated anterior to motor area in the superolateral and medial surfaces of the hemisphere. The premotor area contributes to motor function by its direct contribution to the pyramidal and other descending motor pathways and by influence on the primary motor cortex.

In general, the primary motor area is the cortex in which execution of movements originates and relatively simple movements are maintained. In contrast, the premotor area programmes skilled motor activity and thus directs the primary motor area in its execution. The premotor and primary motor areas are together referred to as the **primary somatomotor area**. Both these areas give origin to corticospinal and corticonuclear fibers and receive fibers from cerebellum after relay in ventral intermediate nucleus of thalamus.

Supplementary motor area: It is predominantly motor in function. This motor area is in the part of area 6 that lies on the medial surface of the hemisphere anterior to the paracentral lobule. It differs from the main motor area in that its stimulation produces bilateral movements.

Motor speech area (Broca's area): This occupies the opercular and triangular portions of the inferior frontal gyrus corresponding to the areas 44 and 45 of Brodmann. This is present on the left side in 98% of right-handed persons. In 70% of left handers, it is again present in left hemisphere. Only in 30%, it is situated in right hemisphere.

Frontal eye field: It lies in the middle frontal gyrus just anterior to precentral gyrus. It is the lower part of area 8 of Brodmann on the lateral surface of cerebral hemisphere, extending slightly beyond that area. Electrical stimulation of this area causes deviation of both the eyes to the opposite side. This is called conjugate movements of the eyes.

Receptive speech area of Wernicke: This is also known as sensory language area. It consists of auditory association cortex and of adjacent parts of the inferior parietal lobule.

Q. 3. Write a note on circulus arteriosus or circle of Willis. (TNMGR, April 2003, 2004)

Ans. It is an arterial circle, situated at the base of brain in the interpuncular fossa. It is formed by the anterior and middle cerebral branches of internal carotid and posterior cerebral branches of basilar artery.

The two anterior cerebral arteries are connected by anterior communicating artery; the middle and posterior cerebral arteries of same side are united by the posterior communicating artery.

The circulus arteriosus attempts to equalize the flow of blood to different parts of brain and provides a collateral circulation in the event of obstruction to one of its components. There is hardly any mixing of blood streams on right and left sides of the circulus arteriosus.

Branches

1. **Cortical or external branches** run on the surface of the cerebrum, anastomose freely and if these get blocked they give rise to small infarcts.
2. **Central branches** perforate the white matter to supply the thalamus, the corpus striatum, and the internal capsule. These do not anastomose and if these get blocked, they give rise to large infarcts.

The central branches are arranged in six groups:

1. **Anteromedial:** The largest branch is called the **medial striate or recurrent artery of Heubner**. It supplies corpus striatum and internal capsule which has motor fibers for face, tongue and shoulder.
2. **Anterolateral:** These are in two groups. The largest branch is called **lenticulostriate or Charcot's artery of cerebral hemorrhage**. It supplies internal capsule which has motor fibers for one side of the body.
3. **Posterolateral or thalamogeniculate:** These are also in two groups. They supply thalamus and geniculate bodies.
4. **Posteromedial** supply thalamus and hypothalamus.

Arterial supply of different areas: Cerebral cortex is supplied by branches of all three cerebral arteries. All the three surfaces receive branches from all three arteries.

Middle cerebral is main artery on superolateral surface.

Anterior cerebral artery is chief artery on medial surface.

Posterior cerebral is principal artery on inferior surface.

13. HUMAN EMBRYOLOGY: HEAD AND NECK

Q. 1. Write a short note on cell cycle. (TNMGR, 2011)

Ans. Multiplication of the somatic (mitosis) and germ (meiosis) cells is the most complex of all cell functions. Mitosis is controlled by genes which encode for release of specific proteins molecules. Mitosis-promoting protein molecules are cyclins A, B and E. Period between the mitosis is called interphase. The cell cycle

is the phase between two consecutive divisions. There are 4 sequential phases in the cell cycle:

1. **G1 (Pre-mitotic gap) phase** is the stage when messenger RNAs for the proteins and the proteins themselves required for DNA synthesis (e.g. DNA polymerase) are synthesized.
2. **S phase** involves replication of nuclear DNA.
3. **G2 (Pre-mitotic gap) phase** is the short gap phase in which correctness of DNA synthesized is assessed.
4. **M phase** is the stage in which process of mitosis to form two daughter cells is completed. This occurs in 4 sequential stages:
 - a. **Prophase:** Each chromosome divides into 2 chromatids which are held together by centromere. The centriole divides and the two daughter centrioles move towards opposite poles of the nucleus and the nuclear membrane disintegrates.
 - b. **Metaphase:** The microtubules become arranged between the two centrioles forming spindle, while the chromosomes line up at the equatorial plate of the spindle.
 - c. **Anaphase:** The centromeres divide and each set of separated chromosomes moves towards the opposite poles of the spindle. Cell membrane also begins to divide.
 - d. **Telophase:** There is formation of nuclear membrane around each set of chromosomes and reconstitution of the nucleus. The cytoplasm of the two daughter cells completely separates.
5. **G0 phase:** The daughter cells may continue to remain in the cell cycle and divide further, or may go out of the cell cycle into resting phase, called G0 phase.

Q. 2. Write a short note on mitosis. (RGUHS, May 2011)

Ans. The period during which the cell is actively dividing is the phase of mitosis. The period between two successive divisions is called interphase, during which DNA content is duplicated.

1. **Prophase:** The chromatin of the chromosome becomes coiled, rod-like appearance. At the end, two chromatids of a chromosome become distinct.
2. **Metaphase:** With the formation of the spindle, chromosomes move to a position midway between the two centrioles, where each chromosome becomes attached to microtubules of the spindle by its centromere.
3. **Anaphase:** The centromere of each chromosome splits longitudinally into two so that the chromatids now become independent chromosomes.
4. **Telophase:** Two daughter nuclei are formed by appearance of nuclear membranes. Chromosomes gradually elongate and become indistinct. Nucleoli

reappear. The centriole is duplicated at this stage or in early interphase.

The division of nucleus is accompanied by the division of the cytoplasm.

Q. 3. Write in detail about meiosis. (TNMGR, April 2012)

Ans. Meiosis consists of two successive divisions called the first and second meiotic divisions. During the interphase preceding the first division, duplication of the DNA content of chromosomes takes place as in mitosis.

First Meiotic Division

The **prophase** of the first meiotic division is prolonged and is usually divided into a number of stages as follows:

- a. **Leptotene:** The chromosomes become visible (as in mitosis), but the chromatids cannot be distinguished at this stage.
- b. **Zygotene:** There are 46 chromosomes in each cell consist of 23 pairs (the X and Y chromosomes of a male being taken as a pair). The two chromosomes of each pair come to lie parallel to each other and are closely apposed. This pairing of chromosomes is also referred to as *synapsis* or *conjugation*. The two chromosomes together constitute a bivalent.
- c. **Pachytene:** The two chromatids of each chromosome become distinct. The bivalent now has four chromatids in it and is called a **tetrad**. There are two central and two peripheral chromatids—one from each chromosome. The two central chromatids (one belonging to each chromosome of the bivalent) become coiled over each other so that they cross at a number of points.
- d. **Diplotene:** The two chromosomes of a bivalent now try to move apart. As they do so, the chromatids involved in crossing over 'break' at the points of crossing and the 'loose' pieces become attached to the opposite chromatid. This results in exchange of genetic material between these chromatids.

The **metaphase** follows. As in mitosis the forty-six chromosomes become attached to the spindle at the equator. The two chromosomes of a pair being close to each other. The **anaphase** differs from that in mitosis in that there is no splitting of the centromeres; one entire chromosome of each pair moves to each pole of the spindle. The resulting daughter cells, therefore, have twenty-three chromosomes, each made up of two chromatids.

The **telophase** is similar to that in mitosis in which two daughter nuclei are formed. The division of nucleus is followed by division of the cytoplasm.

Second Meiotic Division

The first meiotic division is followed by a short interphase. This differs from the usual interphase in that there is no duplication of DNA. The second meiotic division is similar to mitosis. At this stage it may be repeated that the forty-six chromosomes of a cell consist of twenty-three pairs, one chromosome of each pair being derived from the mother and one from the father. During the first meiotic division the chromosomes derived from the father and those derived from the mother are distributed between the daughter cells entirely at random. This, along with the phenomenon of crossing over, results in thorough shuffling of the genetic material so that the cells produced as a result of various meiotic divisions have a distinctive genetic content. A third step in this process of genetic shuffling takes place at fertilization when there is a combination of randomly selected spermatozoa and ova.

Q. 4. Write a note on germinal layers and their derivatives. (TNMGR, Oct. 2012)

Ans. Formation of germ layers: At a very early stage in development, the embryo proper acquires the form of a three-layered disc. This is called the **embryonic disc** (also called **embryonic area**, **embryonic shield** or **germ disc**). The three germ layers that constitute this embryonic disc are:

1. Endoderm (endo = inside).
2. Ectoderm (ecto = outside).
3. Mesoderm (meso = in the middle).

All tissues of the body are derived from one or more of these layers.

Derivatives of Ectoderm

1. **Lining epithelia:** The epithelium lining of the following is of ectodermal origin:
 - a. Skin, including its pigment cells (from neural crest cells).
 - b. Mucous membrane of lips, cheeks, gums, part of the floor of the mouth, part of the palate, nasal cavities and paranasal sinuses.
 - c. Lower part of anal canal.
 - d. Terminal part of male urethra.
 - e. Outer surface of labia minora and whole of labia majora.
 - f. Anterior epithelium of cornea, epithelium of conjunctiva, epithelial layers of ciliary body and iris.
 - g. Outer layer of tympanic membrane, epithelial lining of membranous labyrinth including the special end organs.

2. Glands

- a. **Exocrine:** Sweat glands, sebaceous glands, parotid (and other salivary glands), mammary gland, lacrimal gland.
- b. **Endocrine:** Hypophysis cerebri, adrenal medulla.

3. Other derivatives

- a. Hair
- b. Nails
- c. Enamel of teeth
- d. Lens of eye; musculature of iris; ciliary muscles (from neural crest); vitreous
- e. Nervous system (brain and spinal cord) including all neurons, neuroglia (except microglia), and Schwann cells (from neural crest)
- f. Pia-arachnoid (from neural crest)
- g. Branchial cartilage (from neural crest)
- h. Substance of cornea, sclera and choroid (from neural crest).

Derivatives of Endoderm

1. **Lining epithelia:** The following lining epithelia are of endodermal origin:
 - a. Epithelium of part of the mouth, part of the palate, tongue, tonsil, pharynx, esophagus, stomach, small and large intestines and upper part of anal canal.
 - b. Epithelium of pharyngotympanic tube, middle ear, inner layer of tympanic membrane, mastoid antrum and air cells.
 - c. Epithelium of respiratory tract.
 - d. Epithelium of gallbladder and extrahepatic duct system; epithelium of pancreatic ducts.
 - e. Epithelium of urinary bladder except trigone (mesoderm); female urethra except part of its posterior wall (mesoderm); male urethra except part of the posterior wall of its prostatic part (mesoderm) and except the part of the penile urethra lying in the glans penis (ectoderm).
 - f. Epithelium of greater part of vagina, vestibule and inner surface of labia minora.
2. **Glands**
 - a. **Endocrine:** Thyroid, parathyroid, thymus, islets of Langerhans.
 - b. **Exocrine:** Liver, pancreas, glands in wall of gastrointestinal tract, greater part of prostate (except inner glandular zone) and its female homologues.

Derivatives of Mesoderm

1. All connective tissues including loose areolar tissue filling the interstices between other tissues, superficial and deep fascia, ligaments, tendons, aponeurosis, and the dermis of the skin.

2. Specialized connective tissues like adipose tissue, reticular tissue, cartilage and bone.
3. Dentin of teeth.
4. All muscles (smooth, striated and cardiac) except the musculature of the iris (ectoderm) and ciliary muscles (neural crest).
5. Heart, all blood vessels and lymphatics, and blood cells.
6. Kidneys, ureters, trigone of bladder, posterior wall of part of the female urethra, posterior wall of upper half of prostatic part of the male urethra, and the inner glandular zone of the prostate.
7. Ovary, uterus, uterine tubes, upper part of vagina.
8. Testis, epididymis, ductus deferens, seminal vesicle, ejaculatory duct.
9. Lining mesothelium of pleural, pericardial and peritoneal cavities and of tunica vaginalis.
10. Lining mesothelium of bursae and joints.
11. Substance of cornea, sclera and choroid.
12. Substance of ciliary body and iris.
13. Dura mater, pia-arachnoid and microglia.
14. Adrenal cortex.

Q. 5. Write a short note on neural crest cells. Write a short note on the aberrations associated with neural crest cells.

(TNMGR, March 2007; RGUHS, Nov. 2011; May 2012)

Ans. At the time when the neural plate is being formed, some cells at the junction between the neural plate and the rest of the ectoderm become specialized (on either side) to form the primordia of the neural crest. With the separation of the neural tube from the surface ectoderm, the cells of the neural crest appear as groups of cells lying along the dorsolateral sides of the neural tube. These neural crest cells soon become free (by losing the property of cell to cell adhesiveness). They migrate to distant places throughout the body. In subsequent development, several important structures are derived from the neural crest. These are:

1. Neurons of the spinal posterior nerve root ganglia.
2. Neurons of the sensory ganglia of the fifth, seventh, eighth, ninth and tenth cranial nerves.
3. Neurons of the sympathetic ganglia.
4. Schwann cells that form the neurolemmal sheaths of all peripheral nerves.
5. The specific cells of the adrenal medulla.
6. Chromaffin tissue.
7. Pigment cells (melanoblasts) of the skin.
8. Pia mater and arachnoid mater.

9. Mesenchyme of the dental papilla and odontoblasts.
10. Cells arising from the cranial part of the neural crest migrate into the mesenchyme of the head and neck and influence development of somatomes. They play an important role in development of musculature of head and formation of face.

Aberrations: Neurocutaneous syndromes

1. Hirschsprung's disease
2. Riley-Day syndrome
3. Neurofibromatosis I
4. Tuberous sclerosis complex
5. Epidermal nevus syndrome
6. Incontinentia pigmenti (Bloch-Sulzberger syndrome)
7. Incontinentia pigmenti achromians (hypomelanosis of Ito)
8. Neurocutaneous melanosis
9. Sturge-Weber syndrome
10. Klippel-Trénaunay-Weber syndrome
11. Waardenburg syndromes: Types I, II, III, and IV.

Q. 6. Write a short note on Meckel's cartilage.

(TNMGR, March 2007, April 2012)

Ans. It is derived from first branchial arch around 41–45th day of intrauterine life. It extends from the cartilaginous otic capsule to the midline or symphysis and provides a template for guiding the growth of the mandible. Major portion of this cartilage disappears and remaining part develops into:

1. Mental ossicles
2. Incus and malleus
3. Spine of the sphenoid
4. Anterior ligament of malleus
5. Sphenomandibular ligament

The ossifying membrane is located lateral to Meckel's cartilage and its accompanying neurovascular bundle. From this primary centre, the ossification spreads below and around the inferior alveolar nerve and its incisive branch and upwards to form a trough for accommodating the developing tooth buds. Spread of the intramembranous ossification dorsally and ventrally forms the body and ramus of the mandible.

As ossification continues, the Meckel's cartilage becomes surrounded and invaded by bone. Ossification stops at the site that will later become the mandibular lingual from where the Meckel's cartilage continues into the middle ear and develops into the auditory ossicles. The sphenomandibular ligament which extends from the lingula of mandible to the sphenoid bone also forms a remnant of the Meckel's cartilage.

Q. 7. Write about development of skull bones.

(TNMGR, Sept. 2008)

Ans. The skull is developed from the mesenchyme surrounding the developing brain. This mesenchyme comes into close relationship with the following structures that also contribute to the development of the skull.

- Cranial to the first cervical somite, there are four occipital somite. The mesenchyme arising from the sclerotomes of these somites helps to form part of the base of the skull in the region of the occipital bone.
- The developing internal ear (otic vesicle), and the region of the developing nose, are surrounded by mesenchymal condensations called the otic and nasal capsules respectively. These capsules also take part in forming the mesenchymal basis of the skull.
- The first branchial arch is closely related to the developing skull. It soon shows two subdivisions, mandibular and maxillary processes.

1. Bones formed in membrane

- Frontal and parietal:** Formed in relation to mesenchyme covering developing brain.
- Maxilla (excluding premaxilla), zygomatic, palatine, part of temporal bone:** Formed by mesenchyme of maxillary process.
- Nasal, lacrimal, vomer:** Formed in the membrane covering the nasal capsule.

2. Bones formed in cartilage: Ethmoid and inferior nasal concha—from cartilage of nasal capsule.**3. Bones formed in membrane and cartilage**

- Occipital:** Interparietal part—membranous and rest by endochondral ossification.
- Sphenoid:** Lateral part of greater wing and pterygoid laminae—membrane, rest in cartilage.
- Temporal:** Squamous and temporal part—membranous. Petrous and mastoid—ossification of cartilage of otic capsule. Styloid process is derived from cartilage of second branchial arch.
- Mandible:** Most of the bone is formed in membrane in the mesenchyme of the mandibular process. The ventral part of Meckel's cartilage gets embedded in the bone. The condylar and coronoid processes are ossified from secondary cartilage that appears in these situations.
- Hyoid bone:** From cartilage of 2nd and 3rd arches.

Q. 8. Write a short note on endochondral and intramembranous ossification. (TNMGR, April 2012)

Ans. Formation of bone: All bone is of mesodermal in origin. The process of bone formation is called ossification. In most parts of the embryo, bone

formation is preceded by the formation of cartilaginous model that closely resembles the bone to be formed. This cartilage is subsequently replaced by (not converted into bone). Such kind of bone formation is called **endochondral ossification**. Bones formed in this way are, therefore, called **cartilage bones**. In some situations (e.g. the vault of the skull), formation of bone is not preceded by formation of a cartilaginous model. Instead, bone is laid down directly in a fibrous membrane. This is called **intramembranous ossification** and these bones are called **membrane bones**. These include the bones of the vault of the skull, the mandible and the clavicle.

Q. 9. Describe briefly the development of face.

(BFUHS, Nov. 2003; Gujarat Uni., Oct. 2004; TNMGR, Sept. 2009; April 2012)

Q. Elaborate facial processes. (TNMGR, Oct. 2013)

Ans. After the formation of the head fold, the developing brain and the pericardium form two prominent bulges on the ventral aspect of the embryo. These bulgings are separated by the stomatodaeum. The floor of the stomatodaeum is formed by the buccopharyngeal membrane, which separates it from the foregut. Soon mesoderm covering the developing forebrain proliferates and forms a downward projection that overlaps the upper part of the stomatodaeum. This downward projection is called the **frontonasal process**.

The pharyngeal arches are laid down in the lateral and ventral walls of the most cranial part of the foregut. The face is derived from the following structures that lie around the stomatodaeum:

- The frontonasal process
- The first pharyngeal (or mandibular) arch of each side.

At this stage, each mandibular arch forms the lateral wall of the stomatodaeum. This arch gives off a bud from its dorsal end. This bud is called the **maxillary process**. It grows ventromedially cranial to the main of the arch which is now called the **mandibular process**. The ectoderm overlying the frontonasal process soon shows bilateral localized thickenings, **nasal placodes** induced by the underlying forebrain. The placodes soon sink below the surface to form **nasal pits**. The pits are continuous with the stomatodaeum below. The edges of each pit are raised above the surface; the medial raised edge is called the **medial nasal process** and the lateral edge is called the **lateral nasal process**.

Lower Lip

The mandibular processes of the two sides grow towards each other and fuse in the midline. The fused mandibular processes give rise to the lower lip, and to the lower jaw.

Upper Lip

1. Each maxillary process now grows medially and fuses, first with the lateral nasal process and then with the medial nasal process. The medial and lateral nasal processes also fuse with each other. In this way the nasal pits (now called external nares) are cut off from the stomatodaeum.
2. Frontonasal process becomes much narrower from side to side, with the result that the two external nares come closer together.
3. The stomatodaeum is now bounded above by the upper lip which is derived as follows.
 - a. The mesodermal basis of the lateral part of the lip is formed from the maxillary process. The overlying skin is derived from ectoderm covering this process.
 - b. The mesodermal basis of the median part of the lip (called **philtrum**) is formed from the frontonasal process. The ectoderm of the maxillary process overgrows this mesoderm to meet that of the opposite maxillary process in the midline. As a result, the skin of the entire upper lip is innervated by the maxillary nerves.
4. The muscles of the face (including those of the lips) are derived from mesoderm of the second branchial arch and are therefore supplied by facial nerve.

Nose

The nose receives contributions from the frontonasal process, and from the medial and lateral nasal processes of the right and left sides. The external nares are formed when the nasal pits are cut off from the stomatodaeum by fusion of the maxillary process with the medial nasal process. The external nares gradually approach each other. This is a result of the fact that the frontonasal process becomes progressively narrower and its deeper part ultimately forms the nasal septum. Mesoderm becomes heaped up in the median plane to form the prominence of the nose. Simultaneously, a groove appears between the region of the nose and the bulging forebrain (which may now be called the **forehead**). As the nose becomes prominent, the external nares come to open downwards instead of forwards. The external form of the nose is thus established.

Cheek

The stomatodaeum bounded above by the maxillary process and below by the mandibular process. These processes undergo progressive fusion with each other to form the cheeks. During formation of the upper lip that the maxillary process fuses with the lateral nasal process. This fusion not only occurs in the region of

the lip but also extends from the stomatodaeum to the medial angle of the developing eye. For some time this line of fusion is marked by a groove called the **naso optic furrow or nasolacrimal sulcus**. A strip of ectoderm becomes buried along this furrow and gives rise to the **nasolacrimal duct**.

Eye

The region of the eye is first seen as an ectodermal thickening, **lens placodes**, which appears on the ventro-lateral side of the developing forebrain, lateral and cranial to nasal placodes. The lens placode sinks below the surface and is eventually cut off from the surface ectoderm. The developing eyeball produces a bulging in this situation. The bulging of the eyes is at first directed laterally, and lies in the angles between the maxillary processes and the lateral nasal processes. The eyelids are derived from folds of ectoderm that are formed above and below the eyes, and by mesoderm enclosed within the folds.

External Ear

The external ear is formed around the dorsal part of the first ectodermal cleft. A series of mesodermal thickenings (often called **tubercles or hillocks**) appear on the mandibular and hyoid arches where they adjoin this cleft. The pinna (or auricle) is formed by fusion of these thickenings.

Developmental Anomalies of the Face (TNMGR, April 2013)

It has been seen that the formation of various parts of the face involves fusion of diverse components. This fusion is occasionally incomplete and gives rise to various anomalies.

1. **Harelip:** The upper lip of the hare normally has a cleft. Hence, the term harelip is used for defects of the lips.
 - a. When one or both maxillary processes do not fuse with the medial nasal process, this gives rise to defects in the upper lip. These may vary in degree and may be unilateral or bilateral.
 - b. Defective development of the lower most part of the frontonasal process may give rise to a midline defect of the upper lip.
 - c. When the two, mandibular processes do not fuse with each other the lower lip shows a defect in the midline. The defect usually extends into the jaw.
2. **Oblique facial cleft:** Non-fusion of the maxillary and lateral nasal process gives rise to a cleft running from the medial angle of the eye to the mouth. The nasolacrimal duct is not formed.

3. Inadequate fusion of the mandibular and maxillary processes with each other may lead to an abnormally wide mouth (**macrostomia**). Too much fusion of the mandibular and maxillary processes with each other may lead to small mouth (**microstomia**).
4. The nose may be bifid. Occasionally one half of it may be absent. Very rarely the nose forms a cylindrical projection, or proboscis jutting out from just below the forehead. This anomaly may sometime affect only one half of the nose and is usually associated with fusion of the two eyes (**cyclops**).
5. The entire first arch may remain underdeveloped on one or both sides, affecting the lower eyelid, the maxilla, the mandible, and the external ear. The prominence of the cheek is absent and the ear may be displaced ventrally and caudally. This condition is called **mandibulofacial dysostosis** or **first arch syndrome**.
6. One half of the face may be underdeveloped or overdeveloped.
7. The mandible may be small compared to the rest of the face resulting in a receding chin (**retrognathia**).
8. Congenital tumors may be present in relation to the face. These may represent attempts at duplication of some parts.
9. The eyes may be widely separated (**hypertelorism**).
10. The lips may show congenital pits or fistulae. The lip may be double.

Q. 10. Write a note on pharyngeal pouches.

(TNMGR, April 2001, Oct. 2012; KUHS, June 2013)

Ans. The foregut is bounded ventrally by the pericardium, and dorsally by the developing brain. Cranially, it is at first separated from the stomatodaeum by the buccopharyngeal membrane. When this membrane breaks down, the foregut opens to the exterior through the stomatodaeum. At this stage, the head is represented by the bulging caused by the developing brain while the pericardium may be considered as occupying the region of the future thorax. The two are separated by the stomatodaeum which is the future mouth. The neck is formed by the elongation of the region between the stomatodaeum and the pericardium. This is achieved, partly, by a 'descent' of the developing heart. However, this elongation is due mainly to the appearance of a series of mesodermal thickenings in the wall of the cranial-most part of the foregut. These are called the **pharyngeal or branchial arches**. In the interval between any two adjoining arches, the endoderm extends outwards in the form of

a pouch (**endodermal or pharyngeal pouch**) to meet the ectoderm which dips into this interval as an ectodermal cleft.

The first arch is also called the **mandibular arch**; and the second, the **hyoid arch**. The third, fourth and sixth arches do not have special names. The fifth arch disappears soon after its formation; so that only five arches remain. The following structures are formed in the mesoderm of each arch.

1. **A skeletal element:** This is cartilaginous to begin with. It may remain cartilaginous, may develop into bone, or may disappear.
2. **Striated muscle:** This is supplied by the nerve of the arch. It may subdivide to form a number of distinct muscles, which may migrate away from the pharyngeal region. When they do so, however, they carry their nerve with them and their embryological origin can thus be determined from their nerve supply.
3. **An arterial arch:** Ventral to the foregut, an artery called the ventral aorta develops. Dorsal to the foregut, another artery called the dorsal aorta, is formed. A series of arterial arches (**aortic arches**) connect the ventral and dorsal aortae. One such arterial arch lies in each pharyngeal arch. In a subsequent development, the arrangement of these arteries becomes greatly modified.

Each pharyngeal arch is supplied by a nerve. In addition to supplying the skeletal muscle of the arch, it supplies sensory branches to the overlying ectoderm and endoderm.

Derivatives of the Skeletal Element

1. The cartilage of the first arch is called **Meckel's cartilage**. The incus and malleus (of the middle ear) is derived from its dorsal end. The ventral part of the cartilage is surrounded by the developing mandible, and is absorbed. The part of the cartilage extending from the region of the middle ear to the mandible disappears but its sheath forms anterior ligament of malleus and sphenomandibular ligament. Mesenchyme of first arch also is responsible for formation of bones such as maxilla, mandible, zygomatic, palatine and part of temporal bone.
2. The cartilage of the second arch forms the following: (**Five 'Ss'**)
 - a. Stapes
 - b. Styloid process
 - c. Stylohyoid ligament
 - d. Smaller cornu of hyoid bone
 - e. Superior part of the body of hyoid bone

3. The following structures are formed from the cartilage of the third arch:
 - a. Greater cornu of hyoid bone
 - b. Lower part of the body of hyoid bone
4. The cartilages of the larynx are derived from the fourth and sixth arches with a possible contribution from the fifth arch.

Nerves and Muscles of the Arches

All the muscles derived from a pharyngeal arch are supplied by the nerve of the arch and can, therefore, be identified by their nerve supply. These nerves also innervate the parts of skin and mucous membrane derived from the arches. Some of the nerves (e.g. glossopharyngeal) have only a small motor component and are predominantly sensory. The first arch has a double nerve supply. The mandibular nerve is the **post-trematic nerve** of the first arch, while the chorda tympani (branch of facial nerve) are the **pre-trematic nerve**. This double innervations are reflected in the nerve supply of the anterior two-thirds of the tongue which are derived from the ventral part of the first arch.

Fate of Ectodermal Clefts

After the formation of the pharyngeal arches, the region of the neck is marked on the outside by a series of grooves, **ectodermal clefts**. The dorsal part of the first cleft (between the first and second arches) develops into the epithelial lining of the external acoustic meatus. The pinna (or auricle) is formed from a series of swellings or hillocks that arise on the first and second arches,

where they adjoin the first cleft. The ventral part of this cleft is obliterated.

The second arch grows much faster than the succeeding arches and comes to overhang them. The space between the overhanging second arch and the third, fourth and sixth arches is called the **cervical sinus**. The lower overhanging border of the second arch fuses with tissues caudal to the arches. The cavity of the cervical sinus is normally obliterated. Part of it may persist and give rise to swellings that lie in the neck, along the anterior border of the sternocleidomastoid. These are called **branchial cysts**, and are most commonly located just below the angle of the mandible. If such a cyst opens onto the surface, it becomes a branchial sinus.

Fate of endodermal pouches: The endodermal pouches take part in the formation of several important organs. These are listed below.

First pouch

- a. Its ventral part is obliterated by formation of the **tongue**.
- b. Its dorsal part receives a contribution from the dorsal part of the second pouch, and these two together forms a diverticulum that grows towards the region of the developing ear. The diverticulum is called the **tubotympanic recess**. The proximal part of this recess gives rise to the auditory tube, and the distal part to the middle ear cavity, including the tympanic antrum.

Second pouch

- a. The epithelium of the ventral part of this pouch contributes to the formation of the tonsil.
- b. The dorsal part takes part in the formation of the tubotympanic recess.

Third pouch: This gives rise to the inferior parathyroid glands, and the thymus.

Fourth pouch: This gives origin to the superior parathyroid glands, and may contribute to the thyroid gland.

Fifth or ultimobranchial pouch: A fifth pouch is seen for a brief period during development. It is generally believed to be incorporated into the fourth pouch. The two together forming the **caudal pharyngeal complex**. The superior parathyroid glands arise from this complex. The complex probably also gives origin to the parafollicular cells of the thyroid gland.

Q. 11. Write a short note on primary and secondary cartilages. (TNMGR, March 2008)

Ans.

1. **Primary cartilage:** Cartilage of the pharyngeal arches is known as primary cartilage. In this the

Arch	Nerve of arch	Muscle of arch
First	Mandibular	1. Medial and lateral pterygoids 2. Masseter 3. Temporalis 4. Mylohyoid 5. Anterior belly of digastric 6. Tensor tympani 7. Tensor palati
Second	Facial	1. Muscles of face 2. Occipitofrontalis 3. Platysma 4. Stylohyoid 5. Posterior belly of digastric 6. Stapedius 7. Auricular muscles
Third	Glossopharyngeal	Stylopharyngeus
Fourth	Superior laryngeal] Muscles of larynx and pharynx
Fifth	Recurrent laryngeal	

chondroblasts are surrounded by a cartilaginous matrix. For example, Meckel's cartilage, cartilages of cranial base.

2. **Secondary cartilage:** It does not develop from the established primary cartilage of the skull. In this the chondroblasts are not surrounded by a cartilaginous matrix. It is formed after and separate from the primary cartilaginous skeleton. For example, condylar cartilage, symphysis, ends of clavicle.

14. HUMAN HISTOLOGY

Q. 1. Write a short note on microscopic structure of spleen. (TNMGR, March 2009)

Ans.

1. The surface of the spleen is covered by serous coat, over the coat.
2. Trabeculae arising from the capsule extend into the substance of the spleen.
3. The capsule and trabeculae are made up of fibrous tissue.
4. The spaces between the trabeculae are composed of reticular network, consisting of reticular cells and macrophages.
5. The interstices of reticulum contain lymphocytes, blood vessels and blood cells.
6. White pulp is made up of lymphocytes that surround arterioles.
7. The red pulp is like a sponge, filled by B- and T-lymphocytes, macrophages, and blood cells and lined by reticular cells.

Q. 2. Write a short note on histology of cartilage.

(TNMGR, Sept. 2008)

Ans. Cartilage is considered as modified connective tissue, with cells distributed in homogeneous ground substance within which fibers are embedded.

Cartilage cells: Chondrocytes lying in lacunae.

Ground substance: Made up of complex molecules containing proteins and carbohydrates.

Fibers: Type II collagen fibers.

Q. 3. Write a short note on histology/microanatomy of bone. (TNMGR, Sept. 2007; April 2013)

Ans. Bone is considered as modified connective tissue, with cells distributed in homogeneous ground substance within which collagen fibers and mineral salts are embedded.

Bone cells: Osteocytes, osteoblasts, osteoclasts cells.

Ground substance: Gelatinous ground substance—glycosaminoglycans, proteoglycans and water.

Fibers: Type I collagen fibers.

Q. 4. Write about histologic picture of lymph node.

Ans. Each lymph node consists of connective tissue framework and numerous cells.

Connective Tissue Framework

1. The lymph node is covered by a capsule consisting of collagen fibers.
2. Multiple septa extend into the node from the capsule.
3. The hilum is occupied by dense fibrous tissue.
4. Fibroblasts are associated with connective tissue framework.

Cells of Lymph Node

1. **Lymphocytes:** Lymphatic nodules are composed of B-lymphocytes. The diffuse lymphoid tissue intervening between nodules is made up of T-lymphocytes.
2. Reticular cells associated with connective tissue framework.
3. Macrophages are present in the lymph sinuses.
4. Endothelial cells lining the blood vessels of lymph nodes.
5. Pericytes and smooth muscle cells present around the blood vessels.

Q. 5. Write a short note on microscopic structure of thyroid gland.

Ans.

1. Thyroid gland is covered by fibrous capsule, with septa dividing the gland into lobules.
2. Each lobule is aggregation of follicles.
3. Each follicle is lined by follicular cells that rest of basement membrane.
4. The follicular cavity is filled by colloid.
5. The spaces between follicles are filled by stroma made up of delicate connective tissue, containing capillaries and lymphatics.
6. C cells or parafollicular cells intervene between follicular cells and the basement membrane.
7. Connective tissue stroma surrounding the follicles contains a dense capillary plexus, lymphatic capillaries and sympathetic nerves.

Dental Anatomy and Dental Histology

1. TEETH DEVELOPMENT AND ABNORMALITIES

Q. 1. Discuss in detail the development of tooth. Elaborate the theories of tooth eruption.

(TNMGR, March 2010)

Q. Write a short note on enamel organ and its function.

(TNMGR, March 2007)

Ans. The teeth are formed in relation to the alveolar process. The epithelium overlying the convex border of this process becomes thickened and projects into the underlying mesoderm. This epithelial thickening is called **dental lamina**. The dental lamina is, in fact, apparent even before the alveolar process itself is defined. As the alveolar process is semicircular in outline the dental lamina is similarly curved. The dental lamina now shows a series of local thickenings, each of which is destined to form one milk tooth. These thickenings are called **enamel organs**. There are ten such enamel organs (five on each side) in each alveolar process. The stages in the formation of an enamel organ and the development of a tooth are as follows (Fig. 2.1):

1. Each enamel organ is formed by localized proliferation of the cells of the dental lamina.
2. As the enamel organ grows downwards into the mesenchyme (of the alveolar process) its lower end assumes a cup-shaped appearance. The cup comes to be occupied by a mass of mesenchyme called the **dental papilla**. The enamel organ and the dental papilla together constitute the **tooth germ**. At this stage the developing tooth looks like a cap—it is, therefore, described as the **cap stage** of tooth development.
3. The cells of the enamel organ that line the papilla become columnar. These are called **ameloblasts**.
4. Mesodermal cells of the papilla that are adjacent to the ameloblasts arrange themselves as a continuous epithelium-like layer. The cells of this layer are called

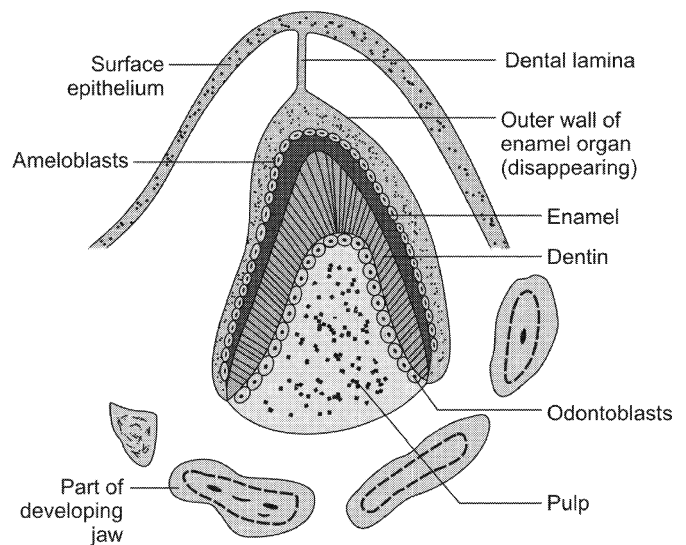


Fig. 2.1: Schematic diagram of tooth development

odontoblasts. The ameloblasts and odontoblasts are separated by a basement membrane. The remaining cells of the papilla form the pulp of the tooth. The developing tooth now looks like a bell (**bell stage**).

5. Ameloblasts lay down enamel on the superficial (outer) surface of the basement membrane. The odontoblasts lay down dentine on its deeper surface. As layer after layer of enamel and dentine are laid down, the layer of ameloblasts and the layer of odontoblasts move away from each other.
6. After the enamel is fully formed, the ameloblasts disappear leaving a thin membrane, the **dental cuticle**, over the enamel. The odontoblasts, however, continue to separate the dentine from the pulp throughout the life of the tooth.
7. The alveolar parts of the maxilla and mandible are formed by ossification in the corresponding alveolar process. As ossification progresses, the roots of the teeth are surrounded by bone. The root of the tooth

is established by continued growth into underlying mesenchyme. Odontoblasts in this region lay down dentin. As layers of dentin are deposited, the pulp space becomes progressively narrower and is gradually converted into a canal through which nerves and blood vessels pass into the tooth. In the region of the root there are no ameloblasts. The dentin is covered by mesenchymal cells that differentiate into cementoblasts. These cells lay down a layer of dense bone called the **cementum**. Still further to the outside, mesenchymal cells form the periodontal ligament which connects the root to the socket in the jaw bone.

The **permanent teeth** are formed as follows:

- The dental lamina gives off a series of buds, one of which lies on the medial side of each developing milk tooth. These buds from enamel organs exactly as described above. They give rise to the permanent incisors, canines and premolars.
- The permanent molars are formed from buds that arise from the dental lamina posterior to the region of the last milk tooth. The dental lamina is established in the 6th week of intrauterine life. At birth the germs of all the temporary teeth and of the permanent incisors, canines and first molars, show considerable development. The germs of the permanent premolars and of the second molars are rudimentary. The germ of the third molar is formed after birth. The developing tooth germs undergo calcification. All the temporary teeth and the permanent lower first molar begin to calcify before birth.

Q. 2. Write a short note on stellate reticulum.

(RGUHS, April 2006)

Ans. Stellate reticulum/enamel pulp: Polygonal cells located in the center of the epithelial organ, begin to separate as more intercellular fluid is produced and form a cellular network, called stellate reticulum. The cells assume a branched reticulum form. The space in between is filled with mucoid fluid, rich in albumin, giving a cushion-like consistency, protecting the delicate enamel forming cells. The cells in the center of the enamel organ are densely packed and form the enamel knot and the vertical extension of the enamel knot is known as enamel cord. Both are temporary structure; act as a reservoir of dividing cells for the growing enamel organ.

Q. 3. Write short note on developmental anomalies in tooth morphology.

(TNMGR, Sept. 2007)

Ans. Anomalies of teeth

- One or more teeth may be absent. Complete absence is called **anodontia**.

- Supernumerary teeth may be present.
- Individual teeth may be abnormal. They may be too large (**macrodont**) or too small (**microdont**).
- Two (or more) teeth may be fused to each other (**gemination**).
- The alignment of the upper and lower teeth may be incorrect (**malocclusion**). This may be caused by one or more of the above anomalies or by defects of the jaws.
- Eruption of teeth may be precocious (i.e. too early). Lower incisors may be present at birth.
- Eruption of teeth may be delayed. The third molar frequently fails to erupt.
- Teeth may form in abnormal situations, e.g. in the ovary or in the hypophysis cerebri.
- There may be improper formation of the enamel (**amelogenesis imperfecta**) or dentin (**dentinogenesis imperfecta**) of the tooth.

Q. 4. Write a short note on theories of tooth eruption.

(TNMGR, April, Oct. 2012; KUHS, June 2013; RUHS, May 2015)

Ans. Tooth eruption is defined as the movement of a tooth from its site of development within the alveolar process to its functional position in the oral cavity.

- Bone remodeling:** Simultaneous bone deposition and bone resorption in the area around tooth causes its axial movement. Given by Brash in 1928.
- Root elongation:** The apical growth of roots results in axial directed force that leads to tooth eruption. Also known as Hammock ligament theory given by Tomes 1872.
- Vascular pressure:** Alteration in local vascular supply and increase in local tissue pressure in PDL leads to tooth eruption.
- Periodontal ligament traction:** The contractility of the fibroblasts present in the PDL provides the force for the tooth eruption. Given by Thomas in 1967.

Other less documented theories of tooth eruptions are:

- Pulp constriction theory (Korff in 1935).
- Dental follicle theory (Marks and Cahill in 1984).
- Growth of periodontal tissues.
- Pressure from muscular action.
- Resorption of alveolar crest.
- Hormonal theory.
- Cellular proliferation theory.

Q. 5. Write a note on factors influencing shedding and eruption of primary teeth.

(TNMGR, Nov. 1995; March 2009)

Ans. Shedding is the physiologic process resulting in the elimination of the deciduous dentition.

Shedding involves resorption of hard and soft tissue. The resorption of hard tissue is achieved by pressure from the erupting successional tooth, as the odontoclasts appears at the site of pressure. The forces of mastication applied to the deciduous teeth are also capable of initiating resorption. In case of soft tissue resorption, apoptotic cell death is involved.

Factors affecting the shedding of primary teeth

1. **Pressure factors:** From erupting permanent teeth, from masticatory forces.
2. Genetic factors.

Factors affecting the eruption of primary teeth

1. Preterm birth.
2. Nutritional deficiencies.
3. Vitamin D resistant rickets.
4. Down syndrome.
5. Physical or mechanical obstruction.
6. Radiation damage.
7. Genetic predisposition.

Q. 6. Write a short note on development of root.

(TNMGR, Sept. 2010; KUHS, June 2013)

Ans. The development of the roots begins after enamel and dentin formation has reached the future cemento-enamel junction (CEJ). The enamel organ forms Hertwig's epithelial root sheath, which molds the shape of roots and initiates radicular dentin formation. Hertwig's epithelial root sheath consists of outer and inner enamel epithelia only. The cells of inner layer remain short and initiate differentiation of odontoblasts, which forms the radicular dentin. Just after this, the Hertwig's epithelial root sheath loses its structural continuity and its remnants persist as epithelial network of strands called **rests of Malassez**.

The root sheath prior to elongation in apical direction forms an epithelial diaphragm, which is a horizontal extension at the future CEJ. Subsequently, the epithelial cells disintegrates and moves away from the surface of dentin so that the connective tissue cells come into contact with outer surface of dentine and differentiate into cementoblasts, that deposit a layer of cementum.

Q. 7. Write about theories of mineralization.

Ans. The various proposed theories of mineralization are:

1. **Robinson's alkaline phosphatase theory:** The enzyme is responsible for mineralization.
2. **Cartier's theory:** According to Cartier alkaline phosphatase has very little role in mineralization and that ATPase is extremely powerful in inducing mineralization.

3. **White and Hers theory:** White and Hers made surprising discovery that bone and especially dentin still possessed possibility of splitting phosphate esters even ion removing and destroying all the enzymes.
4. **pH of cartilage explaining mineralization:** One of the oldest suggestion for mechanism of mineralization is that pH of cartilage is higher than that of other tissues which would favor precipitation of calcium phosphate
5. **Seeding mechanism:** According to this mechanism, there are certain substances called seeding or nucleating having resemblance to apatite. These substances act as mould or template upon which crystals are laid down, after which crystallization proceeds automatically. This process is known as **epitaxy**. The following substances have been considered as possible seeding substances—collagen, chondroitin sulphate, lipid substances, phosphoproteins.
6. **Matrix vesicle concept:** Matrix vesicles are organelles of cellular origin that can be observed electron microscopically in the matrix of cartilage, bone, and other hard tissue.

2. OCCLUSION AND SKULL BONE DEVELOPMENT

Q. 1. Write about development of occlusion from birth to adolescence.

(BFUHS, May 2010; KUHS, Nov. 2015)

Ans. Periods of occlusal development:

1. **Pre-dental period:** During this period, neonates have no teeth. It lasts for 6 months after birth. It has following features:
 - a. **Gum pads:** The alveolar process at the time of birth is known as gum pads. They are horseshoe shape, pink and firm, and develop in two parts: (i) Labio-buccal portion, (ii) lingual portion, separated from each other by dental groove. Each gum pad is divided into ten segments, each containing deciduous tooth sac, by **transverse grooves**. The gingival groove separates gum pad from palate and floor of mouth. Transverse groove between canine and first deciduous molar segment is called **lateral sulcus**. The upper gum pad is both wider and longer than lower gum pad. On closing, contact occurs in the first molar region, and space exists anteriorly (infantile open bite), which helps in suckling.
 - b. **Status of dentition:** Neonates are without teeth for about 6 months. Initially there is crowding of developing teeth, but during first year of life, they

grow rapidly, allowing the proper alignment of teeth.

2. **Deciduous dentition period:** From 6 months to 2–3 years.

The sequence of eruption is: A-B-D-C-E.

Between 3 and 6 years of age, the dental arch is relatively stable. Other normal features during this period are:

- a. Physiological or developmental spacing.
 - b. Flush terminal plane.
 - c. Deep bite.
3. **Mixed dentition period:** It starts with eruption of first permanent molar (6 years). It has been classified into 3 phases:
 - i. **First transitional period:** Emergence of first permanent molar and exchange of the deciduous incisors with permanent incisors. The permanent incisors are larger than deciduous, the excess space needed than present is called **incisal liability** (for maxillary—7 mm and for mandibular arch—5 mm). This is compensated by:
 - a. Utilization of interdental spaces seen in primary dentition.
 - b. Increase in inter-canine width.
 - c. Change in incisor inclination.
 - ii. **Inter-transitional period:** Both upper and lower arches consist of sets of deciduous and permanent teeth, this phase is relatively stable.
 - iii. **Second transitional period:** In this phase, there is replacement of deciduous molars and canines by premolars and permanent cuspids respectively. The space difference between combined width of deciduous canine and molars and mesiodistal width of permanent canine and premolars (**leeway space of Nance**) is greater in mandibular arch, which is utilized for mesial drift of mandibular molars.

Ugly duckling stage: It is transient or self correcting malocclusion seen in maxillary incisor region between 8 and 9 years of age, seen during the eruption of permanent canines.

4. **The permanent dentition period:** The eruption sequence of permanent dentition in maxillary arch: 6-1-2-4-3-5-7 or 6-1-2-3-4-5-7.

The eruption sequence of permanent dentition in mandibular arch: 6-1-2-3-4-5-7 or 6-1-2-4-3-5-7.

Q. 2. Write about prenatal and postnatal growth of cranial base. (TNMGR, Sept. 2009)

Ans.

A. Prenatal Growth

The earliest evidence of formation of the cranial base is seen in the post or late somitic period (4th–8th week of intrauterine life). During this period mesenchymal tissue derived from the primitive streak, neural crest and occipital sclerotomes condense around the developing brain. Thus, a capsule is formed around the brain called **ectomenix** or **ectomeningeal capsule**. The basal portion of this capsule gives rise to the future cranial base. From around the 40th day onwards, this ectomeningeal capsule is slowly converted into cartilage. This heralds the onset of cranial base formation. The conversion of mesenchymal cells into cartilage or chondrification occurs in 4 regions:

1. **Parachordal:** The chondrification centers forming around the cranial end of the notochord are called parachordal cartilages.
2. **Hypophyseal:** Cranial to the termination of notochord, the hypophyseal pouch develops which gives rise to the anterior lobe of the pituitary gland. On either side of the hypophyseal stem, two hypophyseal (postsphenoid) cartilages develop, which fuse together to form the posterior part of the body of sphenoid.

Cranial to the pituitary gland, two presphenoid or trabecular cartilages develop which fuse together and form the anterior part of the body of sphenoid. Anteriorly, the presphenoid cartilage forms mesethmoid cartilage which gives rise to the perpendicular plate of ethmoid and cristagalli.

Lateral to the pituitary gland, chondrification centers are seen which form the lesser wing (orbitosphenoid) and greater wing (alisphenoid) of sphenoid.

3. **Nasal:** Initially during development, a capsule is seen around the nasal sense organ. This capsule chondrifies and forms the cartilages of the nostrils, which fuse with the cartilages of the cranial base.
4. **Otic:** A capsule is seen around the vestibulocochlear sense organs. This capsule chondrifies and later ossifies to give rise to the mastoid and petrous portions of the temporal bone. The otic cartilages also fuse with the cartilages of the cranial base.

The initially separate centers of cartilage formation in the cranial base fuse together into a single irregular and greatly perforated cranial base. The early establishment of the various nervous, blood vessels, etc., from and to the brain results in numerous perforations or foramina in the developing cranial base. The ossifying chondrocranium meets the ossifying desmocranium (cranial vault) to form the neurocranium.

Chondrocranial ossification: The cranial base, which is now in a cartilaginous form, undergoes ossification. The bones of the cranial base undergo both endochondral as well as intramembranous ossification.

Occipital bone: Both endochondral and intramembranous ossification from 7 centers.

Temporal bone: The temporal bone ossifies both endochondrally and intramembranously from 11 centers.

Ethmoid bone: This bone shows only endochondral ossification. It ossifies from three centers.

Sphenoid bone: This bone ossifies both intramembranously and endochondrally. There are at least 15 ossification centers.

B. Postnatal Growth of the Cranial Base

The cranial base grows postnatally by complex interaction between the following three growth processes:

1. **Cortical drift and remodeling:** The cranium is divided into a number of compartments by bony elevation and ridges present in the cranial base. These elevated ridges and bony partitions show bone deposition, while the predominant part of the floor shows bone resorption. This intracranial bone resorption helps in increasing the intracranial space to accommodate the growing brain. The foramina that allow the passage of nerves and blood vessels undergo drifting by bone deposition and resorption so as to constantly maintain their proper relationship with the growing brain.
2. **Elongation at the synchondroses:** Most of the bones of the cranial base are formed by a cartilaginous process. Later the cartilage is replaced by bone. However, certain bands of cartilage remain at the junction of various bones. These areas are called **synchondroses**. The important synchondroses found in the cranial base are:
 - a. Spheno-occipital synchondrosis.
 - b. Sphenoethmoid synchondrosis.
 - c. Intersphenoid synchondrosis.
 - d. Intraoccipital synchondrosis.
 - a. **Spheno-occipital synchondrosis:** It is the cartilaginous junction between the sphenoid and the occipital bones. It is considered to be the most important growth site of the cranial base. It is believed to be active up to the age of 12–15 years. The sphenoid and the occipital segments then become fused in the midline area by 20 years of age. As endochondral bone growth occurs at the spheno-occipital synchondrosis, the sphenoid and occipital bones increase in length and width.

- b. **Spheno-ethmoid synchondrosis:** This is a cartilaginous band between the sphenoid and ethmoid bones. It is believed to ossify by 5–25 years of age.

- c. **Intersphenoidal synchondrosis:** It is a cartilaginous band between the 2 parts of the sphenoid bone. It is believed to ossify at birth.

- d. **Intraoccipital synchondrosis:** This ossifies by 3–5 years of age.

3. **Sutural growth:** The cranial base has a number of bones that are joined to one another by means of sutures. Some of the sutures that are present include:

- a. Sphenofrontal
- b. Frontotemporal
- c. Sphenoethmoid
- d. Frontoethmoid
- e. Frontozygomatic

As the brain enlarges during growth, bone formation occurs at the ends of the bone.

Timing of cranial base growth

- a. By birth, 55–60% of adult size is attained
- b. By 4–7 years, 94% of adult size is attained
- c. By 8–13 years, 98% of adult size is attained.

Q. 3. Discuss the prenatal and postnatal growth of maxilla and mandible.

(TNMGR, March 2007; Sept. 2008)

Ans. Around the 4th week of intrauterine life, a prominent bulge appears on the ventral aspect of the embryo corresponding to the developing brain. Below the bulge, a shallow depression corresponding to the primitive mouth appears, called stomodeum. The floor of the stomodeum is formed by the buccopharyngeal membrane that separates the stomodeum from the foregut.

The mesoderm covering the developing forebrain proliferates and forms a downward projection that overlaps the upper part of stomodeum. This downwards projection is called **frontonasal process**. The mandibular arches of both the sides form the lateral walls of the stomodeum. The mandibular arch gives off a bud from its dorsal end called the **maxillary process**. The maxillary process grows ventromedial—cranial to the main part of the mandibular process. Thus at this stage, the stomodeum is overlapped from above by the frontal process, below by the mandibular process and on the either side by the maxillary processes.

As the maxillary process undergoes growth, the frontonasal process becomes narrow so that the two nasal pits come closer. The line of fusion of the maxillary process and the medial nasal process corresponds to the nasolacrimal duct.

Development of Palate

The palate is formed by contributions of the:

- a. Maxillary process
- b. Palatal shelves given off by the maxillary process
- c. Frontonasal process

Ossification of Palate

Ossification of the palate occurs from the 8th week of intrauterine life. This is an intramembranous type of ossification. The palate ossifies from a single centre derived from the maxilla. The most posterior part of the palate does not ossify. This forms the soft palate. The mid-palatal suture ossifies by 12–14 years.

Development of Maxillary Sinus (RGUHS, Oct. 2010), Discussed in Anatomy (Page No. 18)

Prenatal embryology of mandible: About the 4th week of intrauterine life, the pharyngeal arches are laid down on the lateral and ventral aspects of the cranial-most part of the foregut that lies in close approximation with the stomodeum. Initially there are six pharyngeal arches, but the fifth one usually disappears as soon as it is formed leaving only five. They are separated by four branchial grooves.

Each of these five arches contains:

1. A central cartilage rod that forms the skeleton of the arch.
2. A muscular component termed as branchiomere.
3. A vascular component.
4. A neural element.

The mandibular arch forms the lateral wall of the stomodeum. It gives off a bud from its dorsal end. This bud is called the **maxillary process**. It grows ventromedially, cranial to the main part of the arch, which is now called the **mandibular process**. The mandibular process of both sides grows towards each other and fuses in the midline. They now form the lower border of the stomodeum, i.e. the lower lip and the lower jaw.

Meckel's cartilage: The Meckel's cartilage is derived from the first branchial arch around the 41st and 45th day of intrauterine life. It extends from the cartilaginous otic capsule to the midline or symphysis and provides a template for guiding the growth of the mandible. A major portion of the Meckel's cartilage disappears during growth and the remaining part develops into the following structures:

1. Mental ossicles
2. Incus and malleus
3. Spine of sphenoid bone
4. Anterior ligament of malleus
5. Sphenomandibular ligament

Endochondral bone formation: Endochondral bone formation is seen only in 3 areas of the mandible:

1. Condylar process
2. Coronoid process
3. Mental region

Condylar process: At about the 5th week of intra-uterine life, an area of mesenchymal condensation can be seen above the ventral part of the developing mandible. This develops into a cone-shaped cartilage by about 10th week and starts ossification by 14th week. It then migrates inferiorly and fuses with the mandibular ramus by about 4 months.

Coronoid process: Secondary accessory cartilages appear in the region of the coronoid process by about the 10–14 week of intrauterine life. This secondary cartilage of coronoid process is believed to grow as a response to the developing temporalis muscle. The coronoid accessory cartilage becomes incorporated into the expanding intramembranous bone of the ramus and disappears before birth.

Mental region: In the mental region, on either side of the symphysis, one or two small cartilages appear and ossify in the 7th month of intrauterine life to form variable numbers of mental ossicles in the fibrous tissues of the symphysis. These ossicles become incorporated into the intramembranous bone when the symphysis ossifies completely during the first year of postnatal life.

Postnatal Growth of Maxilla

The growth of the nasomaxillary complex is produced by the following mechanisms:

1. **Displacement:** Maxilla is attached to the cranial base by means of a number of sutures. Thus, the growth of the cranial base has a direct bearing on the nasomaxillary growth. A passive or secondary displacement of the nasomaxillary complex occurs in a downward and forward direction as the cranial base grows. In addition, a primary type of displacement is also seen in a forward direction. This occurs by growth of the maxillary tuberosity in a posterior direction. This results in the whole maxilla being carried anteriorly.
2. **Growth at sutures:** The maxilla is corrected to the cranium and cranial base by a number of sutures. These sutures include:
 - a. Frontonasal suture
 - b. Frontomaxillary suture
 - c. Zygomaticotemporal suture
 - d. Zygomaticomaxillary suture
 - e. Pterygopalatine suture

These sutures are all oblique and more or less parallel to each other. This allows the downward and forward repositioning of the maxilla as growth occurs at these sutures.

3. **Surface remodeling:** In addition to the growth occurring at the sutures, massive remodeling by bone deposition and resorption occurs to bring about:
- Increase in size
 - Change in shape of bone
 - Change in functional relationship

The following are the bone remodeling changes that are seen in the nasomaxillary complex.

Resorption occurs on the lateral surface of the orbital rim leading to lateral movement of the eyeball. To compensate, there is bone deposition on the medial rim of the orbit and on the external surface of the lateral rim. The floor of the orbit faces superiorly, laterally and anteriorly. Surface deposition occurs here and results in growth in a superior, lateral and anterior direction. Bone deposition occurs along the posterior margin of the maxillary tuberosity. This causes lengthening of the dental arch and enlargement of the anteroposterior dimension of the entire maxillary body. This helps to accommodate the erupting molars. Bone resorption occurs on the lateral wall of the nose leading to an increase in size of the nasal cavity. Bone resorption is seen on the floor of the nasal cavity. To compensate there is bone deposition on the palatal side. Thus, a net downward shift occurs leading to increase in maxillary height. The zygomatic bone moves in a posterior direction. This is achieved by resorption on the anterior surface and deposition on the posterior surface. The face enlarges in width by bone formation on the lateral surface of the zygomatic arch and resorption on its medial surface. The anterior nasal spine prominence increases due to bone deposition. In addition, there is resorption from the periosteal surface of labial cortex. As a compensatory mechanism, bone deposition occurs on the endosteal surface of the labial cortex and periosteal surface of the lingual cortex. As the teeth start erupting, bone deposition occurs at the alveolar margins. This increases the maxillary height and the depth of the palate. The entire wall of the sinus except the mesial wall undergoes resorption. This results in increase in size of the maxillary antrum.

Postnatal Growth of Mandible (KUHS, Jan. 2014)

The basal bone or the body of the mandible forms one unit, to which is attached the alveolar process, the coronoid process, the condylar process, the angular process, the ramus, the lingual tuberosity and chin.

Ramus: Resorption occurs on the anterior part of the ramus while bone deposition occurs on the posterior region. This results in a 'drift' of the ramus in the posterior direction.

Corpus or the body of the mandible: The displacement of the ramus results in the conversion of former ramal bone into the posterior part of the body of the mandible. In this manner the body of the mandible lengthens.

Angle of the mandible: On the lingual side of the angle of mandible, resorption takes place on the postero-inferior aspect while deposition occurs on the antero-superior aspect. On the buccal side, resorption occurs on the antero-superior part while deposition takes place on the posterosuperior part. This result in flaring of the angle of the mandible as age advances.

The lingual tuberosity: The combination of resorption in the lingual fossa and deposition on the medial surface of the tuberosity itself accentuates the prominence of the lingual tuberosity.

The alveolar process: As the teeth erupt the alveolar processes develop and increase in height by bone deposition at the margins. The alveolar bone adds to the height and thickness of the body of the mandible.

The chin: The mental protuberance forms by bone deposition during childhood. Its prominence is accentuated by bone resorption that occurs in the alveolar region above it, creating a concavity.

The condyle: The mandibular condyle has been recognized as an important growth site. There are two schools of thought regarding the role of the condylar.

- It was earlier believed that growth occurs at the surface of the condylar cartilage by means of bone deposition. Thus, the condyle grows towards the cranial base. As the condyle pushes against the cranial base, the entire mandible gets displaced forwards and downwards.
- It is now believed that the growth of soft tissues including the muscles and connective tissue carries the mandible forwards away from the cranial base. Bone growth follows secondarily at the condyle to maintain constant contact with the cranial base. The condylar growth rate increases at puberty reaching a peak between 12 and 14 years. The growth ceases around 20 years of age.

The coronoid process: The growth of the coronoid process follows the enlarging the 'V' principle. Viewing the longitudinal section of coronoid process from the posterior aspect, it can be seen that deposition occurs

on the lingual surface of the left and right coronoid process. Although additions take place on the lingual side, the vertical dimension of the coronoid process also increases. This follows the 'V' principle.

Q. 4. Write a note on methods of studying growth.

(RGUHS, May 2006)

Ans. According to profit

a. Measurement approaches

1. *Craniometry*: It is based on the measurements of skull of human skeletal remains.
2. *Anthropology*: It is measured in living individuals by using soft tissue points overlying bony landmarks.
3. *Cephalometric radiography*: This is based on precise orientation of head before a cephalostat.
4. *Comparative anatomy*: It is carried out through comparisons with other species.

b. Experimental approaches

1. *Vital staining*: It involves administration of dyes to the experimental animals. Dyes used are alizarin red 5, trypan blue, and lead acetate.
2. *Radioisotopes*: Technetium-33, Calcium-45, Potassium-32.
3. Metallic implants.
4. Natural markers.

3. DEVELOPMENT OF DENTAL TISSUES

Q. 1. Explain the formation, structure, chemical composition and physical properties of enamel.

Ans.

A. Physical Properties

1. Enamel forms a protective covering of 2–2.5 mm thickness over the crown.
2. It is the hardest calcified tissue in the human body.
3. The specific gravity is 2.8.
4. Its color varies from yellowish white to grayish white.

B. Chemical Properties

Inorganic material: 96%, organic substance and water: 4%.

C. Structure

1. Enamel is composed of enamel rods (5–12 million).
2. In cross section the rods are hexagonal in shape.
3. Each enamel rod is built up of segments separated by dark lines.
4. Generally the rods are directed at right angles to the dentin surface.

5. The change in the direction of rods produces alternating dark and light strips (**Hunter-Schreger bands**).
6. Successive apposition of enamel during formation produces brownish bands (**incremental lines of Retzius**).

D. Life Cycle of Ameloblasts

According to their functions, ameloblasts can be divided into following stages:

1. Morphogenic
2. Organizing
3. Formative
4. Maturative
5. Protective
6. Desmolytic

Q. 2. Write a short note on amelogenesis.

(TNMGR, March 2009)

Ans. Amelogenesis or development of enamel consists of two phases:

a. Formation of enamel matrix: The ameloblasts begin their secretory activity when a small amount of dentin has been laid down. The projection of ameloblasts into enamel matrix is called Tomes process. Two ameloblasts are involved in the synthesis of each enamel rod. The newly formed enamel matrix has two proteins: Amelogenin and enamelin.

b. Mineralization and maturation: Two stages

1. *First stage*: Immediate partial mineralization occurs in the matrix segment and in the interprismatic substance.
2. *Second maturation stage*: Gradual completion of mineralization. It starts from the height of crown and progresses cervically. Each rod matures from the depth to the surface, and the sequence of maturing rods is from cusps or incisal edge toward the cervical line.

Q. 3. Write a short note on age changes in enamel.

(TNMGR, March 2009; HP, May 2015)

Ans. Age changes in enamel

1. Attrition or wear of occlusal surfaces and proximal contact points as a result of mastication.
2. Generalized loss of enamel rod ends.
3. Flattening of perikymata.
4. Finally complete disappearance of perikymata.
5. Localized increase of nitrogen and fluorine.
6. Teeth become darker.
7. Increase in resistance to decay.
8. Reduced permeability.

Q. 4. Write a short note on events in dentinogenesis with its anomalies. (RGUHS, Oct. 2010)

Ans.

- a. **Formation of collagen matrix:** Dentinogenesis begins at the cusp tips after the odontoblasts have differentiated and begin collagen production. Odontoblasts change their shape and size and give rise to several processes, which joins together and becomes enclosed in a tubule. Collagen matrix formation continues, till the formation of crown and root formation. Initial dentin deposition along the cusp tips is known as Korff's fibers. The odontoblasts secrete both the collagen and other components of extracellular matrix.
- b. **Mineralization:** The earliest crystal deposition is in the form of very fine plates of hydroxyapatite on the surface of collagen fibrils and in the ground substance, subsequently within the fibrils.

Anomalies of dentin formation

1. Dentinogenesis imperfecta
2. Dentin dysplasia
3. Regional odontodysplasia.

Q. 5. Write a short note on age changes in dentin. (TNMGR, March 2009; Oct. 2012; HP, May 2015)

Ans.

1. **Formation of secondary dentin:** This is dentin formed after root completion. It is formed at slow rate and contains less number of tubules than primary dentin. It protects the pulp from exposure in older teeth.
2. **Formation of reparative dentin:** This is formed when odontoblasts die during any operative procedure, erosion, dental caries, from the newly formed odontoblasts from underlying undifferentiated perivascular cells in the deeper pulpal tissue. It has fewer tubules and more twisted.
3. **Dead tracts:** Due to any mechanical injury the odontoblastic process may be lost, which appears black in transmitted light and white in reflected light.
4. **Sclerotic or transparent dentin:** Any external stimulus sometimes leads to increase deposition of collagen fibers and apatite crystals in the tubules, leading to complete obliteration.

Q. 6. Write a short note on dentin hypersensitivity. (RGUHS, Oct. 2008; TNMGR, March 2011; Oct. 2013)

Ans. Theories of dentinal hypersensitivity

1. **Direct neural stimulation:** A stimulus reaches the nerve endings in the inner dentin.

2. **Fluid or hydrodynamic theory:** Any stimuli can affect the fluid movements in the dentinal tubules, this fluid movements further stimulates the pain mechanism in the tubules by mechanical disturbances of the nerves closely associated with the odontoblasts and its process (most popular).
3. **Transduction theory:** This theory presumes that the odontoblasts process is the primary structure excited by the stimulus and impulse is transmitted to the nerve endings in the inner dentin.

Q. 7. Write a short note on pain receptors in dental pulp. (TNMGR, April 2012)

Ans.

1. **Non-myelinated nerves:** Sympathetic, found in close association with blood vessels, vasoconstriction.
2. **Large myelinated fibers:** 5–13 μm , mediate the sensation of pain caused by external stimuli.
3. Small myelinated fibers.
4. **Parietal layer of nerves or plexus of Rashkow:** Formed of myelinated and non-myelinated fibers.

Q. 8. Discuss functions of pulp and its response to various stimuli. (TNMGR, April 2013)

Ans. Functions of pulp

1. **Inductive:** Induces oral epithelium to differentiate into dental lamina and enamel organ.
2. **Formative:** It produces dentin through odontoblasts.
3. **Nutritive:** It nourishes the dentin, by means of its rich vascular supply.
4. **Protective:** It responds to various types of stimuli.
5. **Defensive or reparative:** It responds to any irritation by forming reparative dentin.

Response of pulp to stimuli: The pulp is highly responsive to any stimuli. Even a slight stimulus will cause inflammatory cell infiltration, hyperemia or localized abscesses. Hemorrhage may be present. The odontoblast layer is either destroyed or greatly disrupted. Compound containing calcium hydroxide induces reparative dentin formation. Closer the restoration to pulp, greater will be the pulp response.

Q. 9. Write a short note on age changes in pulp. (TNMGR, March 2009; KUHS, Jan. 2014)

Ans.

1. Decrease in number as well as size of pulp cells with aging.
2. Increase fibrosis in the pulpal tissue.
3. Appearance of atherosclerotic plaques and calcification in the pulpal vessels.
4. Formation of pulp stones or denticles.
5. Formation of diffuse calcifications in the pulp chamber.

Q. 10. Write a short note on calcifications of pulp.

(TNMGR, Oct. 2012)

Q. Write a short note on pulp stones.

(BFUHS, Nov. 2007)

Ans.

Diffuse calcifications: They appear as irregular calcific deposits in the pulp tissue, usually following collagenous fiber bundles or blood vessels. The pulp chamber may appear normal, with these calcifications in the roots. These calcifications may be classified as dystrophic calcifications.

Pulp stones (denticles): Nodular, calcified masses appearing in either or both the coronal and root portions of the pulp organ. They are usually asymptomatic. True denticles are similar in structure to dentin, as they have dental tubules. They are rare and usually located close to the apical foramen. False denticles do not exhibit dentinal tubules. They appear as concentric layers of calcified tissue. Pulp stones may be classified as free, attached or embedded. Pulp stones may appear close to blood vessels and nerve trunks. Their incidence as well as size increases with age. They are found more commonly in the coronal pulp.

Q. 11 Write a short note on cementum.

(TNMGR, Oct. 2013)

Ans. Cementum is the mineralized dental tissue covering the anatomic roots of human teeth. It consists of 45–50% inorganic substances and 50–55% organic component. It is formed by connective tissue cells (cementoblasts) of dental follicles, which comes in the contact of newly formed radicular dentin. It is light yellow in color and softer than dentin.

Classification

1. **Cellular cementum:** It contains cementocytes; more frequent on the apical half.
2. **Acellular cementum:** Devoid of cementocyte; more frequent on coronal half of the root.

Cemento-enamel Junction

1. **Cementum overlaps enamel:** 60% of the teeth.
2. **Cementum meets enamel in a sharp line:** 30% of the teeth.
3. **Cementum and enamel does not meet at all:** 10% of the teeth.

Functions

1. It furnishes a medium for the attachment of collagen fibers that bind the tooth to alveolar bone.
2. It serves as major reparative tissue for root surfaces.
3. It helps in functional adaptation of teeth.

Q. 12. Write a short note on cementogenesis.

(RGUHS, Nov. 2011)

Ans. Cementum formation is preceded by deposition of dentin along the inner aspect of Hertwig's epithelial root sheath. The newly formed dentin comes in the contact of connective tissue of dentin follicle, forming the cementoblast. Cementoblasts synthesize collagen and protein polysaccharides, which make up the cementum matrix. After this, the mineralization of the matrix starts, by deposition of calcium and phosphate ions present in the tissue fluids.

Q. 13. Write about role of cementum in health and diseases.

(Suman Vidyapeeth, April 2010)

Ans.**A. Cementum in Health**

Cementum is formed throughout life and is resistant to resorption. Cementum functions as an area of attachment for the periodontal ligament fibers.

1. **Thickness of cementum:** The thickness of cementum varies considerably: Coronal third may be 16–60 μm thick; apical third and furcation areas can be 150–200 μm or even thicker. It is thicker in distal surfaces than in mesial surfaces.
2. **Chemical composition:** 45–50% inorganic substance, 50–55% organic material and water. The inorganic portion consists of calcium and phosphate in the form of hydroxyapatite. The organic portion of the cementum is composed primarily of type I (90%) and type III collagen.
3. **Cells:** Cementoblasts and cementocytes.
4. **Cementogenesis:** Already explained above.
5. **Classification:** Based on the location:
 - a. Coronal cementum.
 - b. Radicular cementum.

Based on the time of formation

- a. **Primary cementum:** Cementum formed before the tooth reaches the occlusal plane.
- b. **Secondary cementum:** Cementum formed after the tooth reaches the occlusal plane.

Based on cellularity

- a. Cellular cementum.
- b. Acellular cementum.

Based on the presence or absence of collagenous fibrils

- a. **Fibrillar cementum:** Cementum with a matrix that contains well defined fibrils of type I collagen.
- b. **Afibrillar cementum:** Cementum that has a matrix devoid of detectable type I collagen fibrils.
 1. **Cemento-enamel junction (CEJ):** Already explained above.

2. **Cementodentinal junction (CDJ):** The terminal apical area of cementum where it joins the internal root canal dentin is known as the CDJ. Width appears to be stable even as age increases. It is about 2–3 μm wide.

B. Cementum in Diseases

1. **Cementum in periodontitis affected teeth:** Cementum affected by periodontitis has a faint mat-like surface texture.
2. **Cementum in periodontal pocket:** The embedded collagen fibers are destroyed in periodontal pocket wall.
3. **Cementum after instrumentation:** Firm instrumentation in the subgingival areas also remove a small amount of cementum resulting in notching of root surface.
4. **Necrotic cementum:** Cementum exposed by apical migration of junctional epithelium is altered by exposure to subgingival plaque within the pocket. It may become hypermineralized, demineralized or necrotic.
5. **Age changes in cementum:** Cementum deposition appears to be continuous throughout life. Cementum deposition is less near CEJ and more in apical areas. Cemental deposition slows in old age.
6. **Developmental and acquired anomalies**
 - a. **Enamel projection:** It occurs in furcation of mandibular teeth. It predisposes the teeth to periodontal defect involving the furcation.
 - b. **Enamel pearls:** This anomaly consists of globules of enamel on the root surface in the cervical region.
 - c. **Cementicles:** These are globular masses of acellular cementum, which form within periodontal ligament.
 - d. **Hypercementosis:** It occurs in abnormal occlusal trauma, unopposed teeth, acromegaly, gigantism, arthritis, Paget's disease, thyroid goiter, vitamin A deficiency.
 - e. **Ankylosis of teeth.**
7. **Cementum related bony pathologies:** Periapical cemental dysplasia, cementoblastoma, cementifying fibroma, cemento-osseous dysplasia, and giantiform cementoma.
8. **Resorption of the cementum:** It occurs in trauma from occlusion, orthodontic tooth movement, pressure from tumor, cyst, embedded teeth, replanted and transplanted teeth, periapical and periodontal pathologies, calcium deficiency, hypothyroidism.

Q.14 Write a short note on development of periodontal ligament.

(MAHE, Dec. 1997; TNMGR, Sept. 2007; BFUHS, Nov. 2007; UHSR, April 2015)

Ans. Development: The Hertwig's epithelial root sheath disintegrates leaving behind the epithelial rests of Malassez. The connective tissue cells of dental follicles come into the contact of newly formed root dentin, and differentiate into cementoblasts, lay down cementum. Other cells of the dental follicle differentiate into fibroblasts, which forms the periodontal ligament.

Q. 15. Write a short note on periodontal ligament (PDL).

(RGUHS, April 2006; TNMGR, March 2010)

Ans. The periodontal ligament is a specialized connective tissue which occupies the space between root and the alveolar bone of the tooth socket. Width range is 0.15–0.38 mm.

Cells of Periodontal Ligament (PDL)

- a. **Synthetic cells:** Osteoblasts, fibroblasts, cementoblasts.
- b. **Resorptive cells:** Osteoclasts, fibroblasts, cementoblasts.
- c. **Other cells:** Epithelial rests of Malassez, mast cells, macrophages.

Fibers of PDL

1. Alveolar crest group
2. Horizontal group
3. Oblique group
4. Apical group
5. Interradicular group

Functions

1. Supportive
2. Sensory
3. Nutritive
4. Homeostatic

Q. 16. Write a short note on alveolar bone.

(TNMGR, March 2007; KLE Uni. Dec. 2008)

Ans. Alveolar process may be defined as that part of the maxilla and the mandible that forms and supports the sockets of the teeth.

- a. **Alveolar bone proper:** Thin lamella of bone that surrounds the root of the tooth.
- b. **Supporting alveolar bone:** Bone that surrounds the alveolar bone proper and gives the support to the socket.

1. *Cortical plates*—compact bone, forming inner and outer plates of the alveolar processes.
2. *Spongy bone*—fills the area between cortical plates and the alveolar bone proper.

Q. 17. Write a short note on bone cells.

(TNMGR, Sept. 2010)

Ans.

1. **Osteoblasts:** Bone forming cells. Formed from the multipotent mesenchymal cells. They secrete type I collagen and matrix. They exhibit a high level of alkaline phosphatase.
2. **Osteoclasts:** Bone resorbing cells. Multinucleated, found in Howship's lacunae, derived from circulating monocytes and local mesenchymal cells.
3. **Osteocytes:** Entrapped osteoblasts in the lacunae are called osteocytes. They resorb the surrounding bone to form spaces called osteocytic lacunae.

Q. 18. Write a short note on bundle bone.

(TNMGR, Sept. 2007)

Ans. The alveolar bone proper consists of lamellated and bundle bone. Bundle bone is that bone in which the principal fibers of the PDL are anchored. The term bundle bone was chosen because the bundles of the principal fibers continue into the bone as Sharpey's fibers. It is characterized by the scarcity of the fibrils in the intercellular substance, which are arranged at right angles to Sharpey's fibers. It contains fewer fibrils than the lamellated bone, and therefore, it appears dark in H&E stained sections. The bundle bone contains more calcium salts per unit area than other types of bone tissues, such areas are seen as dense radiopacities (lamina dura), radiographically.

Q. 19. Write short note on lamina dura.

(TNMGR, Oct. 2013)

Ans. Lamina dura (LD) is a radiographic landmark viewed largely on periapical radiographs (PR). The terminology LD (or alveolus) is applied to the thin layer of dense cortical bone, which lines the roots of sound teeth. The term lamina dura or "hard layer" is derived from the fact that it is more radiopaque than the adjacent bone. Presence of LD is an indication of the health of the teeth. Radiographically it is seen as a thin radiopaque line running around the length of the roots. Adjacent to the LD, on the tooth side, a thin dark shadow represents the space occupied by the periodontal membrane, known as periodontal space. The presence or absence of LD and PDL space on radiographs may also be affected by any variations in the angulations of the X-ray beam. The convexity or concavity of proximal tooth surfaces, the curvature of

the roots, the level of the cemento-enamel junction and the thickness of the alveolar bone may also cause variations in the thickness and clarity of the LD.

4. ORAL MUCOUS MEMBRANE

Q. 1. Write a note on oral mucous membrane in health and diseases.

(TNMGR, April 2013)

Q. Write a short note on oral mucosa.

(KLE, June 2007; TNMGR, Oct. 2012)

Ans. It is a protective lining of the oral cavity consisting partly of epithelium and partly of connective tissue. Anatomically, it begins at the vermilion border of the lip and extends up to a point where the pharynx ends.

Oral Mucous Membrane in Health

Role of oral mucosa

1. It is protective mechanically against both compressive and shearing forces.
2. It provides barrier to various pathogens.
3. It has a role in immunological defense.
4. Minor salivary glands within the mucosa provide lubrication and buffering as well as secretion of some antibodies.
5. The mucosa is richly innervated, providing inputs for touch, properception, pain and taste.
6. Reflexes such as gagging, salivation are initiated by receptors in the oral mucosa.

Development: Primitive oral cavity develops by fusion of embryonic stomatodaeum with foregut after rupture of buccopharyngeal membrane. Structures from branchial arches like tongue, epiglottis and pharynx covered by epithelium are derived from endoderm. Epithelium covering palate, cheeks and gingivae are of ectodermal in origin.

Oral mucosa can be divided into:

- a. **Masticatory mucosa:** Gingiva and hard palate.
- b. **Lining or reflecting mucosa:** Lip, cheek, vestibular fornix, alveolar mucosa, floor of mouth, soft palate.
- c. **Specialized mucosa:** Dorsum of the tongue, taste buds.

It consists of surface epithelium and underlying connective tissue, lamina propria.

- a. **The epithelium:** Derived from the ectoderm. It can be keratinized, nonkeratinized.

Keratinized epithelium consists of four layers

1. **Stratum basale:** Cells are cuboidal or low columnar, adjacent to basement membrane, most active mitotically.

2. *Stratum spinosum* (prickle cell layer): Spherical or elliptical cells.
3. *Stratum granulosum*: Flat and wide cells.
4. *Stratum corneum* (surface layer): Flat cells devoid of nuclei.

Nonkeratinized epithelium: In this stratum corneum and stratum granulosum are absent. It includes lips, buccal mucosa, alveolar mucosa, soft palate, ventral surface of tongue, floor of mouth.

Parakeratinized epithelium: Surface cells have pyknotic nuclei; in this stratum corneum and stratum granulosum are absent.

b. The lamina propria: It has

1. *Papillary layer*: Large finger-like projections.
2. Reticular layer.

Oral Mucous Membrane in Disease

The basic considerations in oral mucosa are variation in tissue color, dryness, smoothness or firmness and bleeding tendency of gingiva.

1. **Periodontal pocket:** It is a pathologically deepened gingival sulcus as a response to plaque toxins and subsequent immunologic response.
2. **Restorative dentistry:** In young patients, when the clinical crown is smaller than the anatomic crown, It is difficult to prepare a tooth for an abutment or crown. The restoration may require replacement when the crown is fully exposed.
3. **Gingival recession:** May result in cemental/root caries and sensitivity of the exposed dentin.
4. **Keratinization of gingiva:** Can be achieved by massage or brushing thus helping in stimulation and minimizing plaque accumulation.
5. **Discoloration of gingiva:** Metal poisoning by lead or bismuth causes characteristic discoloration.
6. Blood dyscrasias can be diagnosed by characteristic infiltration of the oral mucosa.
7. Viral diseases like measles manifest as typical lesions of oral mucosa.
8. **Changes of tongue:** In scarlet fever, atrophy of lingual mucosa causes peculiar redness of strawberry tongue. Systemic diseases such as vitamin deficiencies lead to typical changes as Magenta tongue and beefy red tongue.
9. **Macule:** A flat spot/stain/dyscoloration of the oral mucosa. Amalgam tattoo, nevus, rash of secondary syphilis.
10. **Papule:** Small rounded pimple like variably colored. White variably patterned elevations of Lichen planus.

11. **Plaque:** Slightly raised clearly demarcated area that may be smooth pebbly cracked or fissured: Leukoplakia and erythroplakia.
12. **Vesicle:** Small circumscribed elevated blister not more than 5 mm in diameter with covering layer of epithelial cells and containing an accumulation of fluid. For example, herpes labialis.
13. **Pustule:** Vesicle predominantly containing pus.
14. **Bulla:** Large vesicle or blister. Pemphigus and drug reactions. May appear white due to necrosis of epithelium forming pseudomembrane.
15. **Ulcer:** Characterized by loss of epithelium yielding a punched out area. Traumatic ulcers, aphthous stomatitis, cancer and tuberculosis.
16. **Fissure:** Narrow linear crack of epidermis with an ulcer at its base, e.g. fissured tongue.
17. **Erosion:** Partial loss of upper layers of epithelium: Toothbrush trauma and erosive lichen planus.
18. **Cyst:** Cavity lined by epithelium containing fluid or cells: Gingival cyst.
19. **Nodule:** Localized elevated mass of tissue projecting from surface: Fibroma and mucocele.
20. **Tumour:** Swelling part of an organ: Inflammatory and developmental or neoplastic. Carcinoma is a malignant tumor of epithelial cells.
21. **Wheal:** Pruritic reddened edematous papule.
22. **Sinus/sinus tract:** Leading from underlying cavity cyst or abscess and opening onto surface.
23. **Scar:** White depressed mark, line or area representing healing after injury: Gingivectomy, apicoectomy, deep inflammation and previous trauma.

Q. 2. Write a short note on salivary immunoglobulins. (TNMGR, March 2010)

Ans. The predominant salivary immunoglobulin is secretory IgA or sIgA. It differs from the serum IgA in that it exists as an 11S dimer consisting of two IgA molecules joined by a J chain, plus a secretory component, whereas serum IgA exists as a 7S monomer. Secretory IgA is a product of two different cell types where plasma cell synthesizes polymeric IgA containing J chain of about 1.5 kD and glandular cell synthesizes a glycoprotein secretory component of 7 kD. Secretory component is a receptor for polymeric IgA containing J chain; the IgA binds to secretory component below the tight junction of glandular epithelial cells and is then transported across to the luminal surface. The presence of secretory component makes IgA resistant to proteolytic enzymes. Purified salivary IgA and IgG fractions have been found with agglutinating activity against oral isolates of α -hemolytic streptococci.

These immunoglobulins are produced locally by plasma cells in connective tissue stroma of the glands. It is the first line of defense of the host against pathogens which invade mucosal surfaces. Salivary IgA antibodies could help oral immunity by preventing microbial adherence, neutralizing enzymes, toxins and viruses; or by acting in synergy with other factors such as lysozyme and lactoferrin. In addition, low levels of salivary IgA have been presented as a risk factor for upper respiratory infection and have also been associated with an increased risk for periodontal disease and caries.

Q. 3. Write about ultrastructure of serous cell.

(TNMGR, April 2011)

Ans. Serous cells are specialized for the synthesis, storage and secretion of proteins. The typical serous cell is pyramidal in shape, with its broad base resting on thin basal lamina and its narrow apex bordering on the lumen. The spherical nucleus is located in the basal region of the cell; occasionally binucleated cells are observed. There is accumulation of secretory granules in the apical cytoplasm. The basal portion of the cytoplasm is filled with ribosome studded endoplasmic reticulum. Golgi apparatus is located apical or lateral to nucleus. Mitochondria are found throughout the cell.

Q. 4. Write a short note on collagen and its degradation.

(TNMGR, March 2009)

Ans. Collagen is a specific, high molecular weight protein, to which is attached a small number of sugars and a heterogeneous collection of small glycoproteins. There are at least 12 different types of collagen, each exhibiting certain specific and unique chemical characteristics. Periodontal ligament is predominantly made up of type I and type II collagen. Collagen macromolecules are rod-like, very long and arranged to form fibrils. These fibrils show a highly ordered periodic banding pattern. The fibrils are packed to form fibres. Collagen fibres are further gathered to form large bundles.

Type I: Bone and scar.

Type II: Cartilage.

Type III: Skin, vessels and granulation tissue.

Type IV: Ligaments and lungs.

Type V: Cell surface, hair and placenta.

Degradation: The degradation of collagen is done by enzyme collagenase. Collagenase is secreted as a proenzyme that is activated by specific neutral proteases. Collagenolysis activity takes place outside the osteoclast and occurs at a specific site on the tropocollagen molecule. The broken fragments of the collagen are further decalcified by other proteases.

Q. 5. Write a short note on gingival crevicular fluid.

(TNMGR, Oct. 2011; RUHS, May 2015)

Ans. Gingival crevicular fluid (GCF) is an inflammatory exudate that can be collected at the gingival margin or within the gingival crevice. Gingival crevicular fluid (GCF) can be found in the physiologic space (gingival sulcus), as well as in the pathological space (gingival pocket or periodontal pocket) between the gums and teeth. In the first case it is a transudate, in the second it is an exudate. The constituents of GCF originate from serum, gingival tissues, and from both bacterial and host response cells present in the aforementioned spaces and the surrounding tissues. The collection and analysis of GCF are the noninvasive methods for the evaluation of host response in periodontal disease. These analyses mainly focus on inflammatory markers, such as prostaglandin E₂, neutrophil elastase and beta-glucuronidase, and on the marker of cellular necrosis-aspartate aminotransferase. Further, the analysis of inflammatory markers in the GCF may assist in defining how certain systemic diseases (e.g. diabetes mellitus) can modify periodontal disease, and how periodontal disease can influence certain systemic disorders (atherosclerosis, preterm delivery, diabetes mellitus and some chronic respiratory diseases).

1. HOMEOSTASIS: FLUID AND ELECTROLYTE BALANCE

Q. 1. Discuss the homeostasis. (TNMGR, March 2010)

Ans. The 'homeostasis' refers to the maintenance of constant internal environment of the body (homeo = same; stasis = standing).

Role of Various Systems of the Body in Homeostasis

Some of the functions in which the homeostatic mechanism is well established are given below:

1. The pH of the extracellular fluid (ECF) has to be maintained at the critical value of 7.4. The tissues cannot survive if it is altered. The respiratory system, blood and kidney help in the regulation of pH.
2. Body temperature must be maintained at 37.5°C. Increase or decrease in temperature alters the metabolic activities of the cells. The skin, respiratory system, digestive system, excretory system, skeletal muscles and nervous system are involved in maintaining the temperature within normal limits.
3. Adequate amount of nutrients must be supplied to the cells. Nutrients are essential for various activities of the cell and growth of the tissues. Digestive system and circulatory system play major roles in the supply of nutrients.
4. Adequate amount of oxygen should be made available to the cells for the metabolism of the nutrients. Simultaneously, the carbon dioxide and other metabolic end products must be removed. Respiratory system is concerned with the supply of oxygen and removal of carbon dioxide. Kidneys and other excretory organs are involved in the excretion of waste products.
5. Many hormones are essential for the metabolism of nutrients and other substances necessary for the cells.
6. Water and electrolyte balance should be maintained optimally. Otherwise it leads to dehydration or water toxicity and alteration in the osmolality of the body

fluids. Kidneys, skin, salivary glands and gastrointestinal tract take care of this.

7. For all these functions, the blood must be normal. Only then, it can transport the nutritive substances, respiratory gases, metabolic and other waste products.
8. Skeletal muscles are also involved in homeostasis. It also helps to protect the organism from adverse surroundings, thus preventing damage or destruction.
9. Central nervous system plays an important role in homeostasis. Sensory system detects the state of the body or surroundings. Brain integrates and interprets the pros and cons of these information and commands the body to act accordingly through motor system so that, the body can avoid the damage.
10. Autonomic nervous system regulates all the vegetative functions of the body essential for homeostasis.

Components of Homeostatic System

Homeostatic system in the body acts through self-regulating devices, which operate in a cyclic manner. This cycle includes four components:

1. Sensors or detectors, which recognize the deviation.
2. Transmission of this message to a control center.
3. Transmission of information from the control center to the effectors for correcting the deviation.
4. Effectors, which correct the deviation.

Mechanism of Action of Homeostatic System

The homeostatic system works by feedback system:

1. **Negative feedback:** The system reacts in such a way as to arrest the change or reverse the direction of change. After receiving a message, effectors send negative feedback signals back to the system. Now, the system stabilizes its own function and makes an attempt to maintain homeostasis. For example, secretion of thyroxine, maintenance of water balance.

2. **Positive feedback:** The system reacts in such a way as to increase the intensity of the change in the same direction. Positive feedback is less common than the negative feedback. For example, during blood clotting, milk ejection reflex, and parturition.

Q. 2. Discuss on fluid and electrolyte balance in post-operative polytrauma patient.

(BFUHS, 2006; TNMGR, Sept. 2007, 2009; HP, May 2012)

Q. Write a note on postoperative fluid replacement.
(HP, May 2015)

Ans. Disturbances in water, electrolyte and acid-base balance are common problems encountered in general, medical and dental practice. Some are trivial, but others are associated with a high mortality and require urgent assessment and treatment. It is imperative to provide adequate preoperative stabilization before general anesthesia to prevent hypotension, renal failure, cardiac dysarrhythmias and other potential intraoperative complications. Postoperative fluid and electrolyte levels must be closely monitored and management modified, sometimes on an hourly basis, if complications develop and alter the expected postoperative course.

Total Body Water (Average)

Adult male—60%
Adult female—55%
Child—65%
Infant—65%
Newborn—75%

Total body water (TBW) decreases with age and obesity. Total body water is distributed in the body as follows:

TBW = 60% of body weight.
ICF = 40% of body weight.
ECF = 20% of body weight.
EVF = 15% of body weight.
IVF = 5% of body weight.

Blood volume: Plasma + RBC = 8% of body weight.

Composition of ECF and ICF

Substance	ECF	ICF
Na ⁺ (mEq/L)	142	10
K ⁺	5	141
Ca ²⁺	5	<1
Mg ²⁺	3	58
Cl ⁻	103	4
HCO ₃ ⁻	28	10
Phosphate	4	75
Glucose (mg%)	90	0–20

Fluids

Types: These are categorized by the clinical situation and type of fluid used:

1. **Crystalloids:** Molecular weight <8,000 daltons.
2. **Colloids:** Molecular weight >8,000 daltons, e.g. serum albumin.
 - a. *Maintenance fluids:* Fluids that are used to meet normal daily requirements in patients unable to consume sufficient water. Most commonly used: Dextrose 5 with 20 mEq/L of KCl.
 - b. *Replacement fluids:* These fluids are formulated to correct body fluid deficits caused by loss or sequestration of nearly isotonic, polyionic body fluids. These fluids are used to acutely replace volume deficits in patients with dehydration, trauma and sepsis. Most common used: Dextran and Ringer's solution.

Goals of Fluid Management

- i. Attain and maintain normal body composition and homeostasis.
- ii. Correct life-threatening imbalances.
- iii. Avoid complications of too rapid correction.
- iv. Integrate fluid and electrolyte therapy with nutritional therapy.

Clinical Approach

1. Identify fluid and electrolyte imbalances and their magnitude.
2. Determine which problems need correction prior to surgery.
3. Determine the daily maintenance of fluids and electrolytes.
4. Anticipate additional losses expected during treatment.
5. Evaluate for renal, cardiac, endocrine and hepatic dysfunction.

Physical Evaluation

Clinical signs and symptoms of fluid imbalance:

1. **CNS:** Sleepiness, apathy, slow responses, anorexia, vomiting, decreased tendon reflexes, coma.
2. **GIT:** Progressive decrease in the food consumption, nausea, vomiting, refusal to eat, diarrhea.
3. **CVS:** Orthostatic hypotension, tachycardia, collapsed peripheral and central veins, weak pulse, cold extremities, absent peripheral pulse (deficit). Increased venous pressure distension of peripheral and central veins, increased cardiac output, loud heart sounds, functional murmurs, high pulse pressure, increased pulmonary second sound, gallop pulmonary edema (excess).

4. **Tissues:** Decreased skin elasticity, atonic muscles, sunken eyes, decreased tongue size with longitudinal wrinkles (deficit). Subcutaneous edema, pulmonary crackles (excess).

5. **Metabolic:** Hypothermia.

Electrolyte Abnormalities

Serum Na⁺: 150 mEq/L (normal)

Hypernatremia: >150; hyponatremia: <135. Normal daily intake: 100–150 mg/day (adult); 2.4 mg/day/kg (infant/child <20 kg).

Determination of serum osmolarity and urine Na⁺ levels will assist in evaluation and treatment. Normal osmolarity is between 280 and 300 mOsm.

Hyponatremia

It is based on the clinical evaluation of the extracellular fluid volume, comparison of calculated and measured plasma osmolarity, and urinary Na⁺ determination. If the measured osmolarity is 10 mOsm/kg greater than the calculated osmolarity significant unmeasured osmotically active solutes are present.

Causes

1. **Hyponatremia with normal or elevated osmolarity:** Hyperglycemia, hyperlipidemia, hyperproteinemia.
2. **Hyponatremia with increased ECF volume:** Glucocorticoid deficiency, vomiting, drugs, hypothyroidism, and hypokalemia.
3. **Hyponatremia with decreased ECF volume:** Gastrointestinal losses, mineralocorticoid deficiency, diuretics, and salt losing nephritis.

Clinical Signs and Symptoms

Lethargy, confusion, seizures, nausea, vomiting, anorexia, muscle cramps, and hypothermia. Symptoms of hyponatremia rarely develop until the serum Na⁺ drops below 120–125 mEq/L.

Treatment

1. Restriction of water intake 0.5 L/day.
2. Treat underlying causes.
3. Patients with severe neurological symptoms: Plasma Na⁺ should be increased more rapidly by giving 100 ml of a 3% NaCl, IV over 1 hour.
4. Repeated every 2–3 hours till plasma Na⁺ is >120 mmol/L.
5. Loop diuretics: To prevent volume overload.
6. Frequent monitoring of plasma Na⁺ and overall fluid balance.

Hypernatremia

Causes

1. **Loss of free water:** Inadequate free water intake, loss of water through skin, GIT and renal loss.
2. **Solute loading:** Inappropriate IV replacement, tube feeding, brainstem injuries.

Clinical Signs and Symptoms

Restlessness, tremors, weakness, delirium, confusion, ataxia, seizures, coma, decreased saliva and tears, dry socket and red mucous membrane, red swollen tongue, flushed skin, oliguria and fever.

Treatment

1. Treating underlying causes.
2. Replacement of water.

Mild: Water 2 liters by mouth/5% dextrose IV 6–12 hours.

Moderate: 5% dextrose, 2–4 litres IV 24 hours.

Severe: 0–9% saline, 1 litre, IV 1 hour; 5% dextrose 4 litre, IV 24 hours; 5% dextrose 2–4 litres, IV + oral water. 24–48 hours.

Maintenance treatment: 5% dextrose + oral water to balance urine and insensible loss until plasma and urea are normal.

Potassium: Normal: 3.5–5.5 mEq/L.

Hyperkalemia: >5.5. **Hypokalemia:** <3.5.

Normal daily intake: 40–60 mEq/L. **Total body K⁺:** 3000–4000 mEq/L.

Hypokalemia

Causes

1. Decreased dietary intake.
2. Increased loss.
3. **Increased intracellular shift:** Alkalosis, insulin, α -agonist, IV glucose.

Clinical Signs and Symptoms

Dysarrhythmias, hypotension, weakness, respiratory failure, rhabdomyolysis, polyuria, concentrating defect, decreased GFR.

Treatment

1. Treat underlying causes.
2. K⁺ salt orally or IV (oral route is safer).
3. Diet rich in K⁺—fruit juices, coffee, milk and animal protein.

Replacement rate: 10 mEq/h in non-emergency situations; 20–40 mEq/h in emergency situations and cardiac monitoring.

Hyperkalemia

Causes

1. Phlebotomy, hemolysis, thrombocytosis, leucocytosis.
2. Increased intake of iatrogenic K^+ .
3. Decreased renal excretion of K^+ .
4. Redistribution to extracellular fluid leading to acidosis, muscle damage and hyperglycemia.

Clinical Signs and Symptoms

Decreased heart rate, heart block, asystole, ventricular failure, weakness, paresthesia, and respiratory failure.

Treatment

Potassium levels more than 7.0 mEq/L or severe symptoms constitute emergency therapy.

1. Inject 10 ml of 10% calcium gluconate over 1 minute.
2. Inject 50 ml of 50% glucose, monitor plasma glucose.
3. Start infusion of 10–20% dextrose 500 ml, 4–6 hrly.
4. Calcium resonium 15–30 g orally.
5. If metabolic acidosis is present infuse sodium bicarbonate 1.26%, 500 ml 6–8 hrly, until the plasma (HCO_3^-) is in normal range. Meanwhile watch for circulatory overload.
6. Correct volume depletion, respiratory acidosis if present.
7. Use hemodialysis/hemofiltration or peritoneal dialysis, if the above fail.

Chloride: Normal intake: 80–140 mEq/24 hr.

Hyperchloremia: Acidosis, respiratory alkalosis, dehydration, diabetes insipidus, medications like acetazolamides, ammonium chloride, and renal tubular acidosis.

Hypochloremia: Metabolic alkalosis, respiratory acidosis, emphysema, adrenal cortical insufficiency, primary aldosteronism, thiazides, and diarrhea.

Treatment: Treat the underlying cause.

Postoperative Fluid and Electrolyte Management

1. Assess losses and gains.
2. Correcting existing deficiencies.
3. Provide for maintenance of water, Na^+ and K^+ are the next necessary to replace in the short term management of a patient's fluid balance.

Transfusion Guidelines

1. Concomitant disease status may dictate early use of blood products rather than IV fluids replacement in traumatized and surgical patients.
2. The following facts should be considered to take a decision to transfuse a patient:
 - i. Intravascular volume
 - ii. Duration of the anemia and the operation
 - iii. Probability of extended blood loss
 - iv. Physiologic condition of the patient
3. Healthy patients with the hemoglobin value more than 10 g% rarely require preoperative transfusion. Those with less than 7 g% due to acute anemia will require red blood cell transfusion.
4. With regard to the surgical patients, blood loss during a procedure is based on percent loss of the estimated blood volume (10% in infants and 15–20% in adults).

Q. 3. Write about regulation of acid–base/electrolyte balance. (TNMGR, Sept. 2008; Oct. 2013)

Ans. Acid–base balance is very important for the homeostasis of the body and almost all the physiological activities depend upon the acid–base status of the body. An acid is the proton donor (the substance that liberates hydrogen ion). A base is the proton acceptor (the substance that accepts hydrogen ion). In spite of continuous production of acids in the body, the concentration of free hydrogen ion is kept almost constant at a pH of 7.4 with slight variations.

Hydrogen Ion and pH

An increase in H^+ ion concentration decreases the pH (acidosis) and a reduction in H^+ concentration increases the pH (alkalosis). An increase in pH by one-fold requires a ten-fold decrease in H^+ concentration. In a healthy person, the pH of the ECF is 7.40 and it varies between 7.38 and 7.42.

Determination of Acid–base Status

The acid–base status in the ECF is determined by indirect method by using Henderson-Hasselbalch equation. In this, to determine the pH of a fluid, the concentration of bicarbonate ions (HCO_3^-) and the CO_2 dissolved in the fluid are measured. Normal acid–base ratio is 1 : 20, i.e. the ratio of 1 part of CO_2 (derived from H_2CO_3) and 20 parts of HCO_3^- .

Regulation of Acid–base Balance

Whenever there is a change in pH beyond the normal range, some compensatory changes occur in the body

to bring the pH back to normal level. The body has three different mechanisms to regulate acid–base status:

1. **By acid–base buffer system:** An acid–base buffer system is the combination of a weak acid and a base—the salt. Buffer system maintains pH by binding with free H^+ .

Types of buffer systems

- i. **Bicarbonate buffer system:** Bicarbonate buffer system is present in ECF (plasma). It consists of carbonic acid (H_2CO_3) which is a weak acid and the HCO_3^- which is a weak base, in the form of salt, i.e. sodium bicarbonate ($NaHCO_3$).
 - ii. **Phosphate buffer system:** This system consists of a weak acid, the dihydrogen phosphate (H_2PO_4) in the form of sodium dihydrogen phosphate (NaH_2PO_4) and the base, hydrogen phosphate (HPO_4) in the form of disodium hydrogen phosphate (Na_2HPO_4). Phosphate buffer system is useful in the intracellular fluid (ICF), in red blood cells or other cells. This is more powerful than bicarbonate buffer system.
 - iii. **Protein buffer system:** Protein buffer systems are present in the blood; both in the plasma and erythrocytes.
 - a. Protein buffer systems in plasma—weak acids in the plasma are:
 - C-terminal carboxyl group, N-terminal amino group and side-chain carboxyl group of glutamic acid.
 - Side-chain amino group of lysine.
 - Imidazole group of histidine.
 - b. Protein buffer system in erythrocytes—hemoglobin is the most effective protein buffer.
2. **By respiratory mechanism:** Lungs play an important role in the maintenance of acid–base balance by removing CO_2 which is produced during various metabolic activities in the body. This CO_2 combines with water to form carbonic acid. Since carbonic acid is unstable, it splits into H^+ and HCO_3^- . Entire reaction is reversed in lungs when CO_2 diffuses from blood into the alveoli of lungs, and CO_2 is blown off by ventilation. When metabolic activities increase, more amount of CO_2 is produced in the tissues and the concentration of H^+ increases. Increased H^+ concentration increases the pulmonary ventilation (hyperventilation) by acting through the chemoreceptor. Due to hyperventilation, the excess of CO_2 is removed from the body.
 3. **By renal mechanism:** Kidney maintains the acid–base balance of the body by the secretion of H^+ and by the retention of HCO_3^- .

Disturbances of acid–base status

- i. **Acidosis:** Acidosis is the reduction in pH (increase in H^+ concentration) below normal range.

It is produced by:

1. Increase in partial pressure of CO_2 in the body fluids particularly in arterial blood.
2. Decrease in HCO_3^- concentration.

- ii. **Alkalosis:** Alkalosis is the increase in pH (decrease in H^+ concentration) above the normal range.

It is produced by:

1. Decrease in partial pressure of CO_2 in the arterial blood.
2. Increase in HCO_3^- concentration.

Since the partial pressure of CO_2 (pCO_2) in arterial blood is controlled by lungs, the acid–base disturbances produced by the change in arterial pCO_2 are called the **respiratory disturbances**.

On the other hand, the disturbances in acid–base status produced by the change in HCO_3^- concentration are generally called the **metabolic disturbances**. Thus, the acid–base disturbances are:

1. **Respiratory acidosis:** Caused by alveolar hypoventilation. During hypoventilation the lungs fail to expel CO_2 , which is produced in the tissues. CO_2 accumulates in blood where it reacts with water to form carbonic acid, which is called respiratory acid. Carbonic acid dissociates into H^+ and HCO_3^- . The increased H^+ concentration in blood leads to decrease in pH and acidosis.

Causes

Hypoventilation: Airways obstruction, lung diseases, respiratory center depression, and neural diseases.

2. **Respiratory alkalosis:** Caused by alveolar hyperventilation. Hyperventilation causes excess loss of CO_2 from the body. Loss of CO_2 leads to decreased formation of carbonic acid and decreased release of H^+ .

Causes

Hyperventilation: Hypoxia, anemia, pulmonary edema, pulmonary embolism, cerebral disturbance, and emotional disturbances.

3. **Metabolic acidosis:** Characterized by excess accumulation of organic acids in the body, which is caused by abnormal metabolic processes.

Causes

- a. **Lactic acidosis:** In circulatory shock.
- b. **Ketoacidosis:** In diabetes mellitus.
- c. **Uric acidosis:** In renal failure.
- d. Acid poisoning.

4. **Metabolic alkalosis:** Caused by loss of excess H^+ resulting in increased HCO_3^- concentration.

Causes:

- Vomiting.
- Cushing syndrome.

Clinical Evaluation of Disturbances in Acid–base Status

Anion gap is an important measure in the clinical evaluation of disturbances in acid–base status. Commonly measured cation is sodium and the unmeasured cations are potassium, calcium and magnesium. Usually measured anions are chloride and bicarbonate. The unmeasured anions are phosphate, sulfate, proteins in anionic form such as albumin and other organic anions like lactate. Difference between concentrations of unmeasured anions and unmeasured cations is called **anion gap**. It is calculated as:

$$\text{Anion gap} = [Na^+] - [HCO_3^-] - [Cl^-] = 144 - 24 - 108 \text{ mEq/L} = 12 \text{ mEq/L}$$

Normal value of anion gap is 9 to 15 mEq/L. It increases when concentration of unmeasured anion increases and decreases when concentration of unmeasured cations decreases.

Q. 4. What are the plasma proteins? What are their functions?

Ans. Plasma proteins are

- Serum albumin
- Serum globulin
- Fibrinogen

Normal Values

Total proteins: 7.3 g/dl (6.4 to 8.3 g/dl)

Serum albumin: 4.7 g/dl

Serum globulin: 2.3 g/dl

Fibrinogen: 0.3 g/dl

Albumin/Globulin Ratio

It is an important indicator of some diseases involving liver or kidney. Normal A/G ratio is 2 : 1.

Functions of Plasma Proteins

- Role in coagulation of blood:** Fibrinogen is essential for the coagulation of blood.
- Role in defense mechanism of body:** Gammaglobulin acts as antibodies (immunoglobulins).
- Role in transport mechanism:** Albumin, α -globulin and β -globulin are responsible for the transport of the hormones, enzymes, etc.
- Role in maintenance of osmotic pressure in blood:** Proteins exert the colloidal osmotic (oncotic) pressure.

5. **Role in regulation of acid–base balance:** Plasma proteins have buffering action.

6. **Role in viscosity of blood:** Plasma proteins provide viscosity to the blood, which is important to maintain the blood pressure.

7. **Role in erythrocyte sedimentation rate:** Globulin and fibrinogen accelerate the tendency of rouleaux formation by the red blood cells.

8. **Role in suspension stability of red blood cells:** During circulation, the red blood cells remain suspended uniformly in the blood. This property of the red blood cells is called the suspension stability. Globulin and fibrinogen help in the suspension stability of the red blood cells.

9. **Role in production of trephane substances:** Trephane substances necessary for nourishment of tissue cells in culture. These substances are produced by leukocytes from the plasma proteins.

10. **Role as reserve proteins:** During fasting, inadequate food intake or inadequate protein intake, the plasma proteins are utilized by the body tissues as the last source of energy.

Q. 5. Discuss regulation of body temperature.

(TNMGR, April 2013)

Q. Write note on role of hypothalamus in temperature regulation.

(PAHER, May 2012)

Ans. The body temperature is regulated by hypothalamus, which sets the normal range of body temperature. The set point under normal physiological conditions is 37°C . Hypothalamus has two centers which regulate the body temperature.

A. Heat Loss Center

Heat loss center is situated in preoptic nucleus of anterior hypothalamus. Stimulation of preoptic nucleus results in cutaneous vasodilatation and sweating. Removal or lesion of this nucleus increases the body temperature.

B. Heat Gain Center

Heat gain is otherwise known as heat production center. It is situated in posterior hypothalamic nucleus. Stimulation of posterior hypothalamic nucleus causes shivering. The removal or lesion of this nucleus leads to fall in body temperature.

Mechanism of Temperature Regulation

- When body temperature increases:** Blood temperature also increases. When blood with increased temperature passes through hypothalamus, it stimulates the thermoreceptors present in the heat

loss center in preoptic nucleus. Now, the heat loss center brings the temperature back to normal by two mechanisms:

1. *Promotion of heat loss*: By increasing the secretion of sweat and by inhibiting sympathetic centers in posterior hypothalamus. This causes cutaneous vasodilatation.
 2. *Prevention of heat production*: By inhibiting mechanisms involved in heat production, such as shivering and chemical (metabolic) reactions.
- ii. **When body temperature decreases**: It is brought back to normal by two mechanisms:
1. *Prevention of heat loss*: Sympathetic centers in posterior hypothalamus cause cutaneous vasoconstriction. This leads to decrease in blood flow to skin and so the heat loss is prevented.
 2. *Promotion of heat production*: (i) shivering, (ii) increased metabolic reactions.

Q. 6. Write a short note on fever. (TNMGR, Sept. 2007)

Ans. Elevation of body temperature above the set point is called **hyperthermia**, **fever** or **pyrexia**. It is the part of body's response to disease. Fever may be beneficial to body and on many occasions, it plays an important role in helping the body fight the diseases, particularly the infections.

Classification of Fever

1. **Low-grade fever**: When the body temperature rises to 38°C to 39°C (100.4°F to 102.2°F)
2. **Moderate-grade fever**: When the temperature rises to 39°C to 40°C (102.2°F to 104°F)
3. **High-grade fever**: When the temperature rises above 40°C to 42°C (104°F to 107.6°F).
4. **Hyperpyrexia**: Hyperpyrexia is the rise in body temperature beyond 42°C (107.6°F). Hyperpyrexia results in damage of body tissues. Further increase in temperature becomes life-threatening.

Causes of Fever

1. Infection
2. Hyperthyroidism
3. Brain lesions
4. Diabetes insipidus

Signs and Symptoms

1. Headache
2. Sweating
3. Shivering
4. Muscle pain

5. Dehydration
6. Loss of appetite
7. General weakness.

Hyperpyrexia may result in

1. Confusion
2. Hallucinations
3. Irritability
4. Convulsions

2. BLOOD

Q. 1. What are the factors of coagulation? Describe the coagulation mechanism and the common deficiency factors which commonly occur.

(MAHE, Dec. 1996; TNMGR, April 2000; March 2008; Pacific Uni., May 2011)

Q. Describe the hemostatic mechanism of the human body. Add a brief note on hemophilia and von Willebrand's disease.

(TNMGR, Sept. 2007, 2009; March 2010; April 2012, 2013; MUHS, June 2015)

Q. Write a note on hemostasis.

(Nagpur Uni., March 1998; TNMGR, March 2009; BFUHS, May, Nov. 2009; KLE Uni. May 2009)

Ans. Coagulation or clotting is defined as the process in which blood loses its fluidity and becomes a jelly-like mass a few minutes after it is shed out or collected in a container.

Factors involved in Blood Clotting

Factor I: Fibrinogen.

Factor II: Prothrombin.

Factor III: Thromboplastin (tissue factor).

Factor IV: Calcium.

Factor V: Labile factor (proaccelerin or accelerator globulin).

Factor VI: Presence has not been proved.

Factor VII: Stable factor.

Factor VIII: Antihemophilic factor (antihemophilic globulin).

Factor IX: Christmas factor.

Factor X: Stuart-Prower factor.

Factor XI: Plasma thromboplastin antecedent.

Factor XII: Hageman factor (contact factor).

Factor XIII: Fibrin-stabilizing factor (fibrinase).

Stages of Blood Clotting (Fig. 3.1)

In general, blood clotting occurs in three stages:

Stage 1. Formation of prothrombin activator

Blood clotting commences with the formation of prothrombin activator, which converts prothrombin into thrombin. Prothrombin activator forms by:

- i. **Intrinsic pathway:** The formation of prothrombin activator is initiated by platelets.

Sequence of events:

- a. During the injury, the blood vessel is ruptured, exposing the collagen beneath the endothelium.
- b. When factor XII (Hageman factor) comes in contact with collagen, it is converted into activated factor XII in the presence of kallikrein and high molecular weight (HMW) kinogen.
- c. The activated factor XII converts factor XI into activated factor XI in the presence of HMW kinogen.

- d. The activated factor XI activates factor IX in the presence of factor IV (calcium).
- e. Activated factor IX activates factor X in the presence of factor VIII and calcium.
- f. When platelet comes in contact with collagen of damaged blood vessel, it gets activated and releases phospholipids.
- g. Activated factor X reacts with platelet phospholipid and factor V to form prothrombin activator. This needs the presence of calcium ions.

- ii. **Extrinsic pathway:** The formation of prothrombin activator is initiated by the tissue thromboplastin.

Sequence of events

- a. Injured tissues releases tissue thromboplastin (factor III).
- b. Glycoprotein and phospholipid components of thromboplastin convert factor X into activated factor X, in the presence of factor VII.

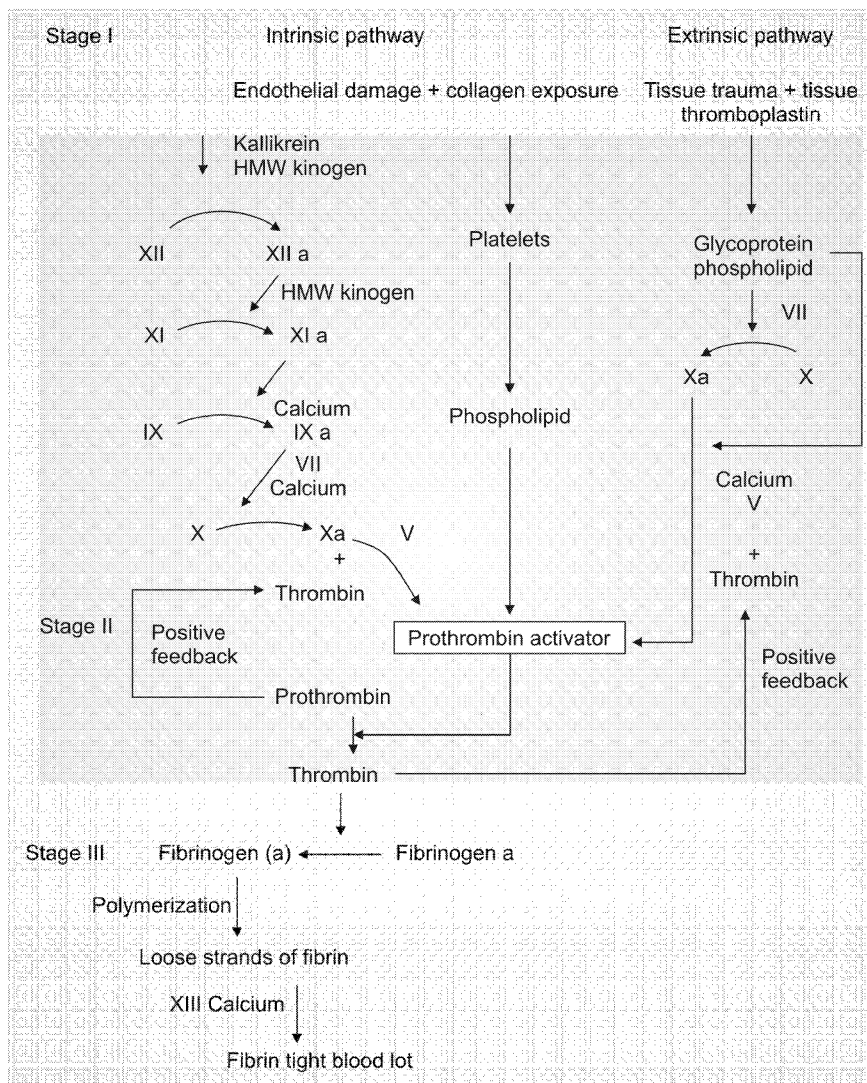


Fig. 3.1: Stages of blood coagulation

- c. Activated factor X reacts with factor V and phospholipid component of tissue thromboplastin to form prothrombin activator. This reaction requires the presence of calcium ions.

Stage 2: Conversion of prothrombin into thrombin

Sequence of events

- i. Prothrombin activator converts prothrombin into thrombin in the presence of calcium.
- ii. Thrombin initiates the formation of more thrombin molecules by positive feedback effect.

Stage 3: Conversion of fibrinogen into fibrin

Sequence of events

- i. Thrombin converts inactive fibrinogen into activated fibrinogen called fibrin monomer.
- ii. Fibrin monomer polymerizes with other monomer molecules and form loosely arranged strands of fibrin.
- iii. These loose strands are modified into dense and tight fibrin threads by fibrin-stabilizing factor (factor XIII) in the presence of calcium ions. All the tight fibrin threads are aggregated to form a meshwork of stable clot.

Applied Physiology

Bleeding Disorders

1. **Hemophilia:** Hemophilia is a group of sex-linked inherited blood disorders, characterized by prolonged clotting time. However, the bleeding time is normal. Usually, it affects the males, with the females being the carriers. Because of prolonged clotting time, even a mild trauma causes excess bleeding which can lead to death. Damage of skin while falling or extraction of a tooth may cause excess bleeding for few weeks. Easy bruising and hemorrhage in muscles and joints are also common in this disease.

Causes of Hemophilia

Hemophilia occurs due to lack of formation of prothrombin activator. The formation of prothrombin activator is affected due to the deficiency of factors VIII, IX or XI.

Types of Hemophilia

Depending upon the deficiency of the factor involved, hemophilia is classified into three types:

- i. **Hemophilia A or classic hemophilia:** Due to the deficiency of factor VIII. 85% of people with hemophilia are affected by hemophilia A.
- ii. **Hemophilia B or Christmas disease:** Due to the deficiency of factor IX. 15% of people with hemophilia are affected by hemophilia B.

- iii. **Hemophilia C or factor XI deficiency:** Due to the deficiency of factor XI. It is a very rare bleeding disorder.

Symptoms of Hemophilia

- i. Spontaneous bleeding.
- ii. Prolonged bleeding due to cuts, tooth extraction and surgery.
- iii. Hemorrhage in gastrointestinal and urinary tracts.
- iv. Bleeding in joints followed by swelling and pain.
- v. Appearance of blood in urine.

Treatment for Hemophilia

Replacement of missing clotting factor.

2. **Purpura:** Purpura is a disorder characterized by prolonged bleeding time. However, the clotting time is normal. Characteristic feature of this disease is spontaneous bleeding under the skin from ruptured capillaries. The hemorrhagic spots under the skin are called purpuric spots (purple-colored patch like appearance). Blood also sometimes collects in large areas beneath the skin which are called ecchymoses. Purpura is classified into three types depending upon the causes:

- i. **Thrombocytopenic purpura:** Due to the deficiency of platelets (thrombocytopenia).
- ii. **Idiopathic thrombocytopenic purpura:** Purpura due to some unknown cause.
- iii. **Thrombasthenic purpura:** Thrombasthenic purpura is due to structural or functional abnormality of platelets.

3. **von Willebrand's disease:** von Willebrand's disease is characterized by excess bleeding even with a mild injury. It is due to deficiency of von Willebrand's factor, which is a protein secreted by endothelium of damaged blood vessels and platelets. This protein is responsible for adherence of platelets to endothelium of blood vessels during hemostasis after an injury. It is also responsible for the survival and maintenance of factor VIII in plasma. Deficiency of von Willebrand's factor suppresses platelet adhesion. It also causes deficiency of factor VIII. This results in excess bleeding, which resembles the bleeding that occurs during platelet dysfunction or hemophilia.

4. **Thrombosis:** Thrombosis or intravascular blood clotting refers to coagulation of blood inside the blood vessels. Normally, blood does not clot in the blood vessel because of some factors which are already explained. But some abnormal conditions cause thrombosis.

Q. 2. Describe RBC's morphology and its variations.

(RGUHS, Nov. 2006; MUHS, June 2011; BFUHS, Nov. 2012)

Ans. Normally, the RBCs are disk-shaped and biconcave (dumbbell shaped).

Advantages of Biconcave Shape of RBCs

1. It helps in equal and rapid diffusion of oxygen and other substances into the interior of the cell.
2. Large surface area is provided for absorption or removal of different substances.
3. Minimal tension is offered on the membrane when the volume of cell alters.
4. Because of biconcave shape, while passing through minute capillaries, RBCs squeeze through the capillaries very easily without getting damaged.

Normal Size

Diameter: 7.2 μ (6.9 to 7.4 μ).

Thickness: At the periphery: 2.2 μ and at the center: 1 μ .

Surface area: 120 μ^2 .

Volume: 85–90 μ^3 .

Normal Structure

Red blood cells are non-nucleated. Other organelles such as mitochondria and Golgi apparatus also are absent in RBC. Red cell does not have insulin receptor. RBC has a special type of **cytoskeleton**, which is made up of **actin** and **spectrin**. Both the proteins are anchored to transmembrane proteins by means of another protein called **ankyrin**.

Variations in Size of Red Blood Cells

1. **Microcytes (smaller cells):** Iron deficiency anemia.
2. **Macrocytes (larger cells):** Megaloblastic anemia.
3. **Anisocytes (cells with different sizes):** Pernicious anemia.

Variations in Shape of Red Blood Cells

1. **Crenation:** Shrinkage as in hypertonic conditions.
2. **Spherocytosis:** Globular form as in hypotonic conditions.
3. **Elliptocytosis:** Elliptical shape as in certain types of anemia.
4. **Sickle cell:** Crescentic shape as in sickle cell anemia.
5. **Poikilocytosis:** Unusual shapes due to deformed cell membrane. The shape will be of flask, hammer or any other unusual shape.

Variations in Structure of Red Blood Cells

1. **Punctate basophilism:** Striated appearance of RBCs by the presence of dots of **basophilic materials**

(porphyrin). It occurs in conditions like **lead poisoning**.

2. **Goblet ring in red blood cells:** Ring or twisted strands of basophilic material appear in the periphery of the RBCs. This appears in the RBCs in certain types of anemia.
3. **Howell-Jolly bodies:** In certain types of anemia; some nuclear fragments are present in the ectoplasm of the RBCs. These nuclear fragments are called Howell-Jolly bodies.

Q. 3. Classify leukocytes. Give an account of leucopoiesis. Mention normal counts of granulocytes and give their functions.

(TNMGR, Nov. 1995; Sept. 2008, 2009; Pacific Uni., May 2012)

Ans. Leukocytes (white blood cells) are the mobile units of the body's protective system. They are formed partially in the bone marrow (granulocytes and monocytes and a few lymphocytes) and partially in the lymph tissue (lymphocytes and plasma cells). After formation, they are transported in the blood to different parts of the body where they are needed.

Classification of Leukocytes**A. Granulocytes**

- i. **Neutrophils (50–70%, 3000–6000/mm³):** Antimicrobial action, anti-inflammatory action, wound-healing, chemotaxis, aggregation of platelets, first line of defense against infection.
- ii. **Eosinophils (2–4%, 150–450/mm³):** Destruction of worms, neurotoxic action, prevention of intravascular clotting, acute hypersensitivity reactions.
- iii. **Basophils (0–1%, 0–100/mm³):** Antimicrobial action, acceleration of inflammatory response.

B. Agranulocytes

- i. **Monocytes (2–6%, 200–600/mm³):** Formation of colony forming blastocytes, aggregation of platelets, chemotaxis, stimulation of phagocytic cells, acceleration of inflammatory response, activation of T cells.
- ii. **Lymphocytes (20–30%, 1500–2700/mm³):** Antimicrobial action, necrosis of tumor, activation of immune system, promotion of inflammation, and chemotaxis.

Q. 4. Write a short note on blood groups and their significance.

(TNMGR, March 2008, 2009; March, Sept 2010; RGUHS, Oct. 2010)

Q. Write a note on importance of blood groups in blood transfusion.

(TNMGR, Sept. 2007; BFUHS, May 2007)

Ans. A and B antigens–agglutinogens

ABO system is based on the presence or absence of antigen A and antigen B. Blood is divided into four groups:

1. 'A' group
2. 'B' group
3. 'AB' group
4. 'O' group

Blood having antigen A belongs to 'A' group. Blood with antigen B and α -antibody belongs to 'B' group. If both the antigens are present, blood group is called 'AB' group and serum of this group does not contain any antibody. If both antigens are absent, the blood group is called 'O' group.

Determination of ABO group: Also called blood grouping, blood typing or blood matching.

Principle of blood typing: Blood typing is done on the basis of agglutination. Agglutination occurs if an antigen is mixed with its corresponding antibody which is called isoagglutinin.

Antigen and antibody present in ABO blood groups:

Group	Antigen in RBC	Antibody in serum	% age of Indian having the blood group
A	A	Anti-B (β)	23
B	B	Anti-A (α)	33
AB	A and B	No antibody	7
O	No antigen	Anti-A and anti-B	37

Importance of ABO Groups in Blood Transfusion

During blood transfusion, only compatible blood must be used. While transfusing the blood, antigen of the donor and the antibody of the recipient are considered. Thus, RBC of 'O' group has no antigen and so agglutination does not occur with any other group of blood. So, 'O' group blood can be given to any blood group persons and the people with this blood group are called '**Universal Donors**'.

Plasma of AB group blood has no antibody. This does not cause agglutination of RBC from any other group of blood. People with AB group can receive blood from any blood group persons. So, people with this blood group are called '**Universal Recipients**'.

Transfusion Reactions Due to ABO Incompatibility

Transfusion reactions occur due to transfusion error that involves transfusion of incompatible (mismatched) blood. The reactions may be mild causing only fever and hives (skin disorder characterized by itching) or may be severe leading to renal failure, shock and death.

In mismatched transfusion, the transfusion reactions occur between donor's RBC and recipient's plasma. So, if the donor's plasma contains agglutinins against recipient's RBC, agglutination does not occur because these antibodies are diluted in the recipient's blood. But, if recipient's plasma contains agglutinins against donor's RBCs, the immune system launches a response against the new blood cells. Donor RBCs are agglutinated resulting in transfusion reactions.

Rh Factor

Rh factor is an antigen present in RBC. The persons having D antigen are called 'Rh positive' and those without D antigen are called 'Rh negative'. Among Indian population, 85% of people are Rh positive and 15% are Rh negative. Rh group system is different from ABO group system because the antigen D does not have corresponding natural antibody (anti-D). However, if Rh positive blood is transfused to an Rh negative person anti-D is developed in that person. On the other hand, there is no risk of complications if the Rh positive person receives Rh negative blood.

Transfusion Reactions due to Rh Incompatibility

When a Rh negative person receives Rh positive blood for the first time, he is not affected much, since the reactions do not occur immediately. But, the Rh antibodies develop within one month. Antibodies developed in the recipient remain in the body forever. So, when this person receives Rh positive blood for the second time, the donor's RBCs are agglutinated and severe transfusion reactions occur immediately.

Hemolytic Disease of Fetus and Newborn: Erythroblastosis Fetalis

It characterized by abnormal hemolysis of RBCs, due to Rh incompatibility. Erythroblastosis fetalis is a disorder in fetus, characterized by the presence of erythroblasts in blood. When a mother is Rh negative and fetus is Rh positive (the Rh factor being inherited from the father), usually the first child escapes the complications of Rh incompatibility. This is because the Rh antigen cannot pass from fetal blood into the mother's blood through the placental barrier. However, at the time of parturition (delivery of the child), the Rh antigen from fetal blood may leak into mother's blood because of placental detachment. During postpartum period, i.e. within a month after delivery, the mother develops Rh antibody in her blood. When the mother conceives for the second time and if the fetus happens to be Rh positive again, the Rh antibody from mother's blood crosses placental barrier and enters the fetal

blood. Rh antibody which enters the fetus causes agglutination of fetal RBCs resulting in hemolysis. Due to excessive hemolysis severe complications develop, viz.

1. Severe anemia
2. Hydrops fetalis
3. Kernicterus

Prevention or Treatment for Erythroblastosis Fetalis

- i. If mother is found to be Rh negative and fetus is Rh positive, anti-D (antibody against D antigen) should be administered to the mother at 28th and 34th weeks of gestation, as prophylactic measure. If Rh negative mother delivers Rh positive baby, then anti-D should be administered to the mother within 48 hours of delivery.
- ii. If the baby is born with erythroblastosis fetalis, the treatment is given by means of exchange transfusion.

Other Blood Groups

1. Lewis blood group
2. MNS blood groups
3. Auberger groups
4. Diego group
5. Bombay group
6. Duffy group
7. Lutheran group
8. P group
9. Kell group
10. I group
11. Kidd group
12. Sulter Xg group

Q. 5. Write functions and applied aspects of platelets.

(TNMGR, March 2002; April 2012; BFUHS, May 2011)

Ans.

1. **Role in blood coagulation:** By forming intrinsic prothrombin activator.
2. **Role in clot retraction:** By releasing contractile proteins, actin, myosin, thrombosthenin.
3. **Role in prevention of blood loss:** By releasing 5-HT, sealing of damaged blood vessels and formation of temporary plugs.
4. **Role in repair of ruptured blood vessel:** By forming platelet derived growth factors.
5. **Role in defense mechanism:** By agglutination of foreign body.

In addition, the platelet membrane contains large amounts of phospholipids that activate multiple stages in the blood clotting process.

Q. 6. Write a short note on composition and functions of blood.

(TNMGR, March 2010; MUHS, June 2011; RGUHS, Nov. 2011)

Q. Write a note on blood components.

(BFUHS, May 2011)

Ans. Blood contains the blood cells which are called formed elements and the liquid portion known as plasma. Three types of cells are present in the blood:

1. Red blood cells (RBCs) or erythrocytes.
2. White blood cells (WBCs) or leukocytes.
3. Platelets or thrombocytes.

Plasma

Plasma is a straw-colored clear liquid part of blood. It contains 91–92% water and 8–9% solids.

a. Solids (7–8%)

i. **Organic substance:** Plasma proteins; amino acids; glucose; fats; hormones; enzymes; and non-protein nitrogenous substances.

ii. **Inorganic substances:** Sodium; calcium; potassium; magnesium, etc.

b. Water (92–93%)

c. **Gases:** Oxygen, carbon dioxide, and nitrogen.

Serum is the clear straw-colored fluid that is left after blood has clotted. Fibrinogen is absent in serum because it is converted into fibrin during blood clotting. Thus, serum = plasma – fibrinogen.

Functions

1. **Nutritive function:** Nutritive substances derived from digested food are absorbed from gastrointestinal tract and carried by blood to different parts of the body for growth and production of energy.
2. **Respiratory function:** It carries oxygen from alveoli of lungs to different tissues and carbon dioxide from tissues to alveoli.
3. **Excretory function:** Waste products formed in the tissues are removed by blood and carried to the excretory organs like kidney, skin, liver, etc. for excretion.
4. **Transport of hormones and enzymes:** Hormones are released directly into the blood. The blood transports these hormones to their target organs/tissues. Blood also transports enzymes.
5. **Regulation of water balance:** Water content of the blood is freely interchangeable with interstitial fluid. This helps in the regulation of water content of the body.
6. **Regulation of acid–base balance:** Plasma proteins and hemoglobin act as buffers and help in the regulation of acid–base balance.

7. **Regulation of body temperature:** Because of the high specific heat of blood, it is responsible for maintaining the thermoregulatory mechanism in the body.
8. **Storage function:** Water and some important substances like proteins, glucose, sodium and potassium are constantly required by the tissues. Blood serves as a ready-made source for these substances.
9. **Defensive function:** Neutrophils and monocytes engulf the bacteria by phagocytosis. Lymphocytes are involved in development of immunity. Eosinophils are responsible for detoxification, disintegration and removal of foreign proteins.

Q. 7. Describe erythropoiesis and factors affecting erythropoiesis. (TNMGR, March 2008)

Q. Elaborate on hematopoiesis. (TNMGR, Oct. 2013)

Ans. Erythropoiesis is the process of the origin, development and maturation of erythrocytes (Fig. 3.2).

Hemopoiesis or hematopoiesis is the process of origin, development and maturation of all the blood cells.

The blood cells begin their lives in the bone marrow from a single type of cell called the **pluripotent hematopoietic stem cell**, from which all the cells of the circulating blood are eventually derived. Then the successive divisions of the pluripotent cells occur to form the different circulating blood cells (Fig. 3.2).

The intermediate stage cells are very much like the pluripotent stem cells, even though they have already become committed to a particular line of cells and are called **committed stem cells**.

The different committed stem cells, when grown in culture, will produce colonies of specific types of blood cells. A committed stem cell that produces erythrocytes is called a colony-forming unit-erythrocyte (CFU-E). Growth and reproduction of the different stem cells are controlled by multiple proteins called growth inducers.

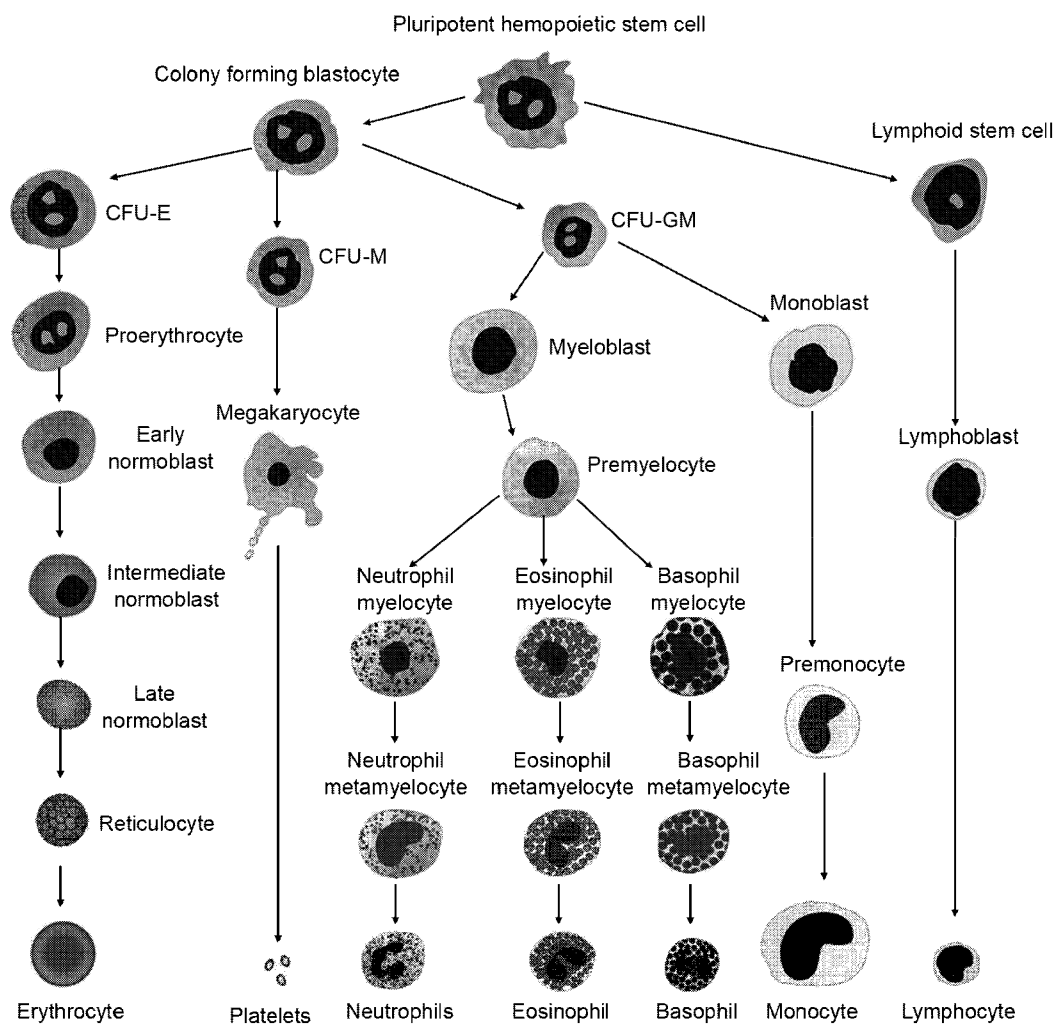


Fig. 3.2: Stages of erythropoiesis. CFU-E: Colony forming unit-erythrocyte, CFU-M: Colony forming unit-megakaryocyte, CFU-GM: Colony forming unit-granulocyte/monocyte

Factors Affecting Erythropoiesis

A. General Factors

1. **Erythropoietin/hemopoietin/erythrocyte stimulating factors:** Production of proerythroblasts, development and release of matured erythrocytes into blood.
2. **Thyroxine:** It accelerates erythropoiesis.
3. **Growth factors:** Induce proliferation of stem cells. interleukin-3; interleukin-6; interleukin-11.
4. **Vitamins:** Vitamins B, C, D, and E.

B. Maturation Factors

1. **Vitamin B₁₂ (cyanocobalamin):** Essential for the synthesis of DNA in RBCs. Also called antipernicious factor.
2. **Intrinsic factor:** Required for the absorption of vitamin B₁₂.
3. **Folic acid:** Essential for the synthesis of DNA in RBCs.

C. Factors Necessary for Hemoglobin Formation

1. First class proteins and amino acids
2. Iron
3. Copper
4. Cobalt and nickel
5. Vitamins

Q. 8. Write about formation of lymph.

(TNMGR, Sept. 2002)

Ans. Lymph is formed from interstitial fluid, due to the permeability of lymph capillaries. When blood passes via blood capillaries in the tissues, 9/10th of fluid passes into venous end of capillaries from the arterial end. And, the remaining 1/10th of the fluid passes into lymph capillaries, which have more permeability than blood capillaries. So, when lymph passes through lymph capillaries, the composition of lymph is more or less similar to that of interstitial fluid including protein content. Proteins present in the interstitial fluid cannot enter the blood capillaries because of their larger size. So, these proteins enter lymph vessels, which are permeable to large particles also.

Addition of proteins and fats: Tissue fluid in liver and gastrointestinal tract contains more protein and lipid substances. So, proteins and lipids enter the lymph vessels of liver and gastrointestinal tract in large quantities. Thus, lymph in larger vessels has more proteins and lipids.

Concentration of lymph: When the lymph passes through the lymph nodes, it is concentrated because of absorption of water and the electrolytes. However, the proteins and lipids are not absorbed.

Composition of lymph: Usually, lymph is a clear and colorless fluid. It is formed by 96% water and 4% solids. Some blood cells are also present in lymph.

Functions of lymph

1. Important function of lymph is to return the proteins from tissue spaces into blood.
2. It is responsible for redistribution of fluid in the body.
3. Bacteria, toxins and other foreign bodies are removed from tissues via lymph.
4. Lymph flow is responsible for the maintenance of structural and functional integrity of tissue. Obstruction to lymph flow affects various tissues, particularly myocardium, nephrons and hepatic cells.
5. Lymph flow serves as an important route for intestinal fat absorption. This is why lymph appears milky after a fatty meal
6. It plays an important role in immunity by transport of lymphocytes.

3. CARDIOVASCULAR SYSTEM

Q. 1. Write a note in cardiopulmonary arrest.

(TNMGR, March 2008; BFUHS, May 2008)

Ans. Cardiac arrest is defined as inability of the heart to sustain an effective output. In cardiac arrest circulation ceases or stops and vital organs are deprived of oxygen.

Etiology

1. Cardiac disease
2. Hypoxia
3. Hypotension
4. Hypoglycemia
5. Fainting
6. **Drugs:** Intravascular injection of adrenalin, sensitivity to local anaesthetics
7. Electrolytic imbalance
8. Vagal reflex mechanism
9. Terminal illness

Diagnosis

1. Absence of pulse in major vessels.
2. Cessation of respiration, absence of breath sounds.
3. Absence of the heart sounds.
4. Pupils may be dilated with sluggish or no reaction to light.
5. Skin may appear pale or cyanosed.
6. In general examination, person is unconscious and not responding to stimuli.

Treatment

Cardiac pulmonary resuscitation (CPR) is most effective, when started immediately and should be initiated by any person present at the time of cardiac arrest.

Q. 2. Write about cardiopulmonary resuscitation.

(TNMGR, March 2009, 2010; HP, July 2011)

Ans. Management of the CPR: Outside the hospital, it is the basic life support (BSL). Inside the hospital, it is BSL plus advanced care life support (ACLS) and post-resuscitation life support, called as cardiac pulmonary cerebral resuscitation (CPCR).

A. Basic Life Support (BSL)

The major objective of BSL is to maintain oxygenation in lungs, brain and heart with rescue breathing and cardiac compression by which oxygen is transported to tissues before the ACLS. The procedure involves maintenance of airway, breathing, and circulation.

1. **Airway:** When the victim is unresponsive, the victim must be made to lie supine, on the firm flat surface. The rescuer should be at the victim's side at a distance equal to the width of the victim's body and at the level of victim's shoulder.

Triple maneuver

- i. Open the mouth—clear the airway.
- ii. Head tilt and chin lift.
- iii. Jaw thrust.

In case of foreign body airway obstruction, following maneuver can be used:

- i. Back blows should be given on the middle of back of the patient. This produces cough reflex.
- ii. Heimlich maneuver consists of manual thrust with the patient breathing, rescuer behind the patient and compressing the patient's chest 6–10 times.
- iii. Finger sweep method.

2. **Breathing:** First determine the presence or absence of breathing by placing the ear near the victim's mouth or nose, looking for the chest wall movement, auscultation of the chest for breath sounds.

Expired air resuscitation:

- i. **Mouth to mouth breathing:** The rescuer uses his expired air oxygen to supply to the victim.
 - a. Open the airway with triple maneuver.
 - b. Close the victim's nostrils with the thumb and index finger.
 - c. Take a deep breath and form a seal with lips around the victim's mouth before exhaling.
 - d. Two slow breaths (1/2 to 2 seconds per puff) are given to provide good chest expansion.

- ii. **Mouth to nose breathing**

- a. Tilt the victim's head back with one hand over the victim's forehead.
- b. Close the victim's mouth.
- c. Lift the victim's lower jaw with the other hand.
- d. Take a deep breath, form a seal with the lips around victim's nose and blow.
- e. Victim's is then allowed to exhale.

- iii. **Mouth to airway breathing**

- a. Close the victim's nostrils with the thumb and index finger.
- b. Take a deep breath and form a seal with the lips around the victim's mouth before exhaling.
- c. Two slow breaths are given to provide good chest expansion.

3. **Circulation:** If no pulse is palpated one should start external cardiac compression to establish circulation.

External cardiac compression: These compressions provide circulation as a result of a generalized increased in intrathoracic pressure, due to direct compression of the heart between the sternum and the vertebrae. When the compressions are accomplished by rescue breathing the blood supplied to the organ is likely to carry oxygen.

- a. Position the victim, supine on the firm surface.
- b. Locate the lower margin of the victim's rib cage.
- c. Locate the lower part of the sternum, by moving the fingers along the notch, where the rib meets the sternum in the center of the chest wall.
- d. Place the heel of one hand, on the lower half of the sternum, with the other hand on the top of the first hand.
- e. For adult, the sternum should be depressed approximately 1/2 to 1 1/2 inches.
- f. Duration of the each compression should be 50% of the compression release cycle with a chest compression rate of 80–100 per minute.

Standard approach to unconscious patient in one rescuer CPR

- a. Open the airway and deliver slow air breaths.
- b. Perform 18 compressions at the rate of two ventilations.
- c. After 5 cycles of compressions, reevaluate the patient.
- d. Check for return of carotid pulse.
- e. If absent, resume CPR.
- f. With two rescuers CPR, the ratio of compression and ventilation is maintained at 5 : 1.

B. Advanced Cardiac Life Support (ACLS)

ACLS helps to evaluate and restore the spontaneous circulatory function.

First ABCD of ACLS

- A—Airway
- B—Breathing
- C—Circulation
- D—Defibrillation

Second ABCD of ACLS

- A—Perform endotracheal intubation.
- B—Assist ventilation.
- C—Circulatory support, gain IV access, attach monitor, identify rhythm, measure blood pressure, and provide appropriate medication.
- D—Differential diagnosis, find and treat the cause.

Postcardiac Arrest Complications

1. **Complications of CPR:** Rib fracture, cardiac laceration, etc.
2. **Ischemic injury:** Renal, cerebral, hepatic, etc.

Outcome of Resuscitation

If the arrest time is less than 6 minutes and CPR time is less than 15 minutes, the outcome is satisfactory. If the arrest time exceeds 6 minutes and CPR time exceeds 15 minutes, chances of survival are almost nil.

Q. 3. Write a note on cardiac cycle.

(TNMGR, April 2000, 2001; HP, July 2011)

Ans. Cardiac cycle is defined as the sequence of **coordinated events** taking place in the heart during each beat. Each heartbeat consists of two major periods called systole and diastole. During systole, heart contracts and pumps the blood through arteries. During diastole, heart relaxes and blood is filled in the heart. All these changes are repeated during every heartbeat, in a cyclic manner.

Events of Cardiac Cycle

1. Atrial events
2. Ventricular events

Divisions and duration of cardiac cycle: When the heartbeats at a normal rate of 72/minute, duration of each cardiac cycle is about 0.8 second.

1. **Atrial events:** Atrial events are divided into two divisions:
 - a. Atrial systole = 0.11 (0.1) sec.
 - b. Atrial diastole = 0.69 (0.7) sec.
2. **Ventricular events:** Ventricular events are divided into two divisions:
 - a. Ventricular systole = 0.27 (0.3) sec.
 - b. Ventricular diastole = 0.53 (0.5) sec.

In clinical practice, the term 'systole' refers to ventricular systole and 'diastole' refers to ventricular

diastole. Ventricular systole is divided into two subdivisions and ventricular diastole is divided into five subdivisions.

Ventricular Systole

1. Isometric contraction = 0.05 second.
2. Ejection period = 0.22 second.

Ventricular Diastole

1. Protodiastole = 0.04 second.
2. Isometric relaxation = 0.08 second
3. Rapid filling = 0.11 second.
4. Slow filling = 0.19 second.
5. Last rapid filling = 0.11 second.

Among the atrial events, atrial systole occurs during the last phase of ventricular diastole. Atrial diastole is not considered as a separate phase, since it coincides with the whole of ventricular systole and earlier part of ventricular diastole.

Q. 4. What is normal cardiac output? Describe the factors regulating cardiac output.

Ans. Cardiac output is the amount of blood pumped from each ventricle. Usually, cardiac output is expressed in three ways:

1. **Stroke volume:** The amount of blood pumped out by each ventricle during each beat. Normal value: 70 ml (60–80 ml).
2. **Minute volume:** The amount of blood pumped out by each ventricle in one minute. Minute volume = stroke volume × heart rate. Normal value: 5 L/ventricle/minute.
3. **Cardiac index:** It is defined as the amount of blood pumped out per ventricle/minute/square meter of the body surface area. Normal value: 2.8 ± 0.3 L/m²/min.

Factors Maintaining Cardiac Output

1. **Venous return:** Venous return is the amount of blood which is returned to heart from different parts of the body. Cardiac output is **directly proportional** to venous return. Venous return depends upon five factors:
 - i. Respiratory pump
 - ii. Muscle pump
 - iii. Gravity
 - iv. Venous pressure
 - v. Sympathetic tone
2. **Force of contraction:** Cardiac output is **directly proportional** to the force of contraction, provided the other three factors remain constant. According to **Frank-Starling law**, force of contraction of heart

is directly proportional to the initial length of muscle fibers, before the onset of contraction. Force of contraction depends upon preload and afterload. Force of contraction of heart and cardiac output are **directly proportional** to preload. Force of contraction of heart and cardiac output are **inversely proportional** to afterload.

3. **Heart rate:** Cardiac output is **directly proportional** to heart rate provided, the other three factors remain constant.
4. **Peripheral resistance:** Peripheral resistance is the resistance or load against which the heart has to pump the blood. So, the cardiac output is **inversely proportional** to peripheral resistance.

Q. 5. Draw and label a normal ECG. Define and describe the different waves of ECG.

(TNMGR, Oct. 2003)

Ans. Electrocardiography is the technique by which electrical activities of the heart are studied. **Electrocardiograph** is the instrument (machine) by which electrical activities of the heart are recorded. **Electrocardiogram** (ECG or EKG from electrocardiogram in Dutch) is the record or graphical registration of electrical activities of the heart, which occur prior to the onset of mechanical activities. Normal ECG consists of waves, complexes, intervals and segments.

Waves of Normal ECG (Fig. 3.3)

Waves of ECG recorded by limb lead II are considered as the typical waves. Normal electrocardiogram has the following waves, namely P, Q, R, S and T.

Major Complexes in ECG

1. 'P' wave—atrial complex.
2. 'QRS' complex—initial ventricular complex.
3. 'T' wave—final ventricular complex.
4. 'QRST'—ventricular complex.

'P' wave: 'P' wave is also called **atrial complex**. 'P' wave is produced due to the **depolarization** of **atrial musculature**. Normal duration of 'P' wave is 0.1 second. Normal amplitude of 'P' wave is 0.1 to 0.12 mV.

Clinical significance: 'P' wave helps in the diagnosis of several cardiac problems such as:

1. **Right atrial hypertrophy:** 'P' wave is tall (more than 2.5 mm) in lead II. It is usually pointed.
2. **Left atrial dilatation or hypertrophy:** It is tall and broad-based or M-shaped.
3. **Atrial extrasystole:** Small and shapeless 'P' wave, followed by a small compensatory pause.

4. **Hyperkalemia:** 'P' wave is absent or small.
5. **Atrial fibrillation:** 'P' wave is absent.
6. **Middle AV nodal rhythm:** 'P' wave is absent.
7. **Sinoatrial block:** 'P' wave is inverted or absent.
8. **Atrial paroxysmal tachycardia:** 'P' wave is inverted.

'QRS' complex: 'QRS' complex is also called the **initial ventricular complex**. 'QRS' complex is due to **depolarization** of **ventricular musculature**. 'Q' wave is due to the depolarization of basal portion of interventricular septum. 'R' wave is due to the depolarization of apical portion of interventricular septum and apical portion of ventricular muscle. 'S' wave is due to the depolarization of basal portion of ventricular muscle near the atrioventricular ring. Normal duration of 'QRS' complex is between 0.08 and 0.10 second.

Clinical significance: Variation in the duration, amplitude and morphology of 'QRS' complex helps in the diagnosis of several cardiac problems such as:

1. **Bundle branch block:** QRS is prolonged or deformed.
2. **Hyperkalemia:** QRS is prolonged.

'T' wave: 'T' wave is the **final ventricular complex**. 'T' wave is due to the **repolarization** of **ventricular musculature**. Normal duration of 'T' wave is 0.2 second.

Clinical significance: 'T' wave helps in the diagnosis of several cardiac problems such as:

1. **Acute myocardial ischemia:** Hyperacute 'T' wave develops. Hyperacute 'T' wave refers to a tall and broad-based 'T' wave, with slight asymmetry.
2. **Old age, hyperventilation, anxiety, myocardial infarction, left ventricular hypertrophy and pericarditis:** 'T' wave is small, flat or inverted.
3. **Hypokalemia:** 'T' wave is small, flat or inverted.
4. **Hyperkalemia:** 'T' wave is tall and tented.

'U' wave: 'U' wave is not always seen. It is also an insignificant wave in ECG. It is supposed to be due to **repolarization** of **papillary muscle**.

Clinical significance: Appearance of 'U' wave in ECG indicates some clinical conditions such as:

1. **Hypercalcemia, thyrotoxicosis and hypokalemia:** 'U' wave appears. It is very prominent in hypokalemia.
2. **Myocardial ischemia:** Inverted 'U' wave appears.

Intervals and Segments of ECG

'P-R' interval: 'P-R' interval is the interval between the onset of 'P' wave and onset of 'Q' wave. 'P-R' interval signifies the atrial depolarization and conduction of impulses through AV node. 'P' wave represents the atrial depolarization.

Normal duration of 'P-R interval' is 0.18 second and varies between 0.12 and 0.2 second.

Clinical significance: 'P-R' interval helps in the diagnosis of several cardiac problems such as:

1. It is prolonged in bradycardia and first degree heart block.
2. It is shortened in tachycardia, Wolf-Parkinson-White syndrome, Lown-Ganong-Levine syndrome, Duchenne muscular dystrophy and type II glycogen storage disease.

'Q-T' interval: 'Q-T' interval is the interval between the onset of 'Q' wave and the end of 'T' wave. 'Q-T' interval indicates the ventricular depolarization and ventricular repolarization, i.e. it signifies the electrical activity in ventricles. Normal duration of Q-T interval is between 0.4 and 0.42 second.

Clinical significance

1. 'Q-T' interval is prolonged in long 'Q-T' syndrome, myocardial infarction, myocarditis, hypocalcemia and hypothyroidism.
2. 'Q-T' interval is shortened in short 'Q-T' syndrome and hypercalcemia.

'S-T' segment: 'S-T' segment is the time interval between the end of 'S' wave and the onset of 'T' wave. It is an isoelectric period.

J point: The point where 'S-T' segment starts is called 'J' point. It is the junction between the QRS complex and 'S-T' segment. Normal duration of 'S-T' segment is 0.08 second.

Clinical significance: Variation in the duration of 'S-T' segment and its deviation from isoelectric base indicates the pathological conditions such as:

1. Elevation of 'S-T' segment occurs in anterior or inferior myocardial infarction, left bundle branch block and acute pericarditis. In athletes, 'S-T' segment is usually elevated.
2. Depression of 'S-T' segment occurs in acute myocardial ischemia, posterior myocardial infarction, ventricular hypertrophy and hypokalemia.
3. 'S-T' segment is prolonged in hypocalcemia
4. 'S-T' segment is shortened in hypercalcemia.

'R-R' interval: 'R-R' interval is the time interval between two consecutive 'R' waves.

Significance: 'R-R' interval signifies the duration of one cardiac cycle. Normal duration of 'R-R' interval is 0.8 second (Fig. 3.3).

Significance of measuring 'R-R interval: Measurement of 'R-R' interval helps to calculate:

1. Heart rate
2. Heart rate variability.

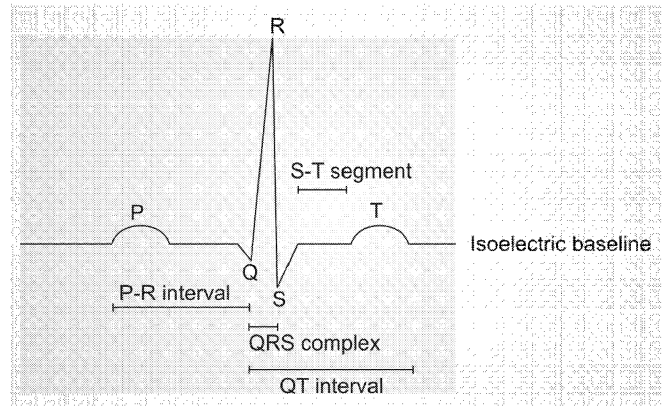


Fig. 3.3: Waves of normal ECG

Q. 6. Define the arterial blood pressure and give its normal values. Describe the mechanism which regulates the blood pressure. Add a note on its importance in dentistry. (TNMGR, April 2000)

Q. Write a note on regulation of blood pressure.

(BFUHS, Oct. 2010)

Ans. Arterial blood pressure is defined as the lateral pressure exerted by the column of blood on wall of arteries. Generally, the term 'blood pressure' refers to arterial blood pressure. Arterial blood pressure is expressed in four different terms:

1. **Systolic blood pressure:** The maximum pressure exerted in the arteries **during systole** of heart. Normal systolic pressure: 120 mm Hg (110 – 140 mm Hg).
2. **Diastolic blood pressure:** The minimum pressure exerted in the arteries **during diastole** of heart. Normal diastolic pressure: 80 mm Hg (60 – 80 mm Hg).
3. **Pulse pressure:** The difference between the systolic pressure and diastolic pressure. Normal pulse pressure: 40 mm Hg (120 – 80 = 40).
4. **Mean arterial blood pressure:** The average pressure existing in the arteries. It is the diastolic pressure plus one-third of pulse pressure.

Determinants of Arterial Blood Pressure

1. Central Factors

1. **Cardiac output:** Systolic pressure is directly proportional to cardiac output.
2. **Heart rate:** Marked alteration in the heart rate affects the blood pressure by altering cardiac output.

II. Peripheral Factors

1. **Peripheral resistance:** Diastolic pressure is directly proportional to peripheral resistance.
2. **Blood volume:** Blood pressure is directly proportional to blood volume.
3. **Venous return:** Blood pressure is directly proportional to venous return.
4. **Elasticity of blood vessels:** Blood pressure is inversely proportional to the elasticity of blood vessels.
5. **Velocity of blood flow:** Blood pressure is directly proportional to the velocity of blood flow.
6. **Diameter of blood vessels:** Blood pressure is inversely proportional to the diameter of blood vessel.
7. **Viscosity of blood:** Blood pressure is directly proportional to the viscosity of blood.

Regulation of Arterial Blood Pressure

I. Nervous Mechanism for Regulation of Blood Pressure

Short-term regulation. Nervous regulation is rapid among all the mechanisms involved in the regulation of arterial blood pressure. The nervous mechanism regulating the arterial blood pressure operates through the vasomotor system.

Mechanism of action of vasomotor center in the regulation of blood pressure: Vasomotor center regulates the arterial blood pressure by causing vasoconstriction or vasodilatation. However, its actions depend upon the impulses, it receives from other structures such as baroreceptor, chemoreceptor, higher centers and respiratory centers.

1. **Baroreceptor mechanism:** Baroreceptor is the receptors, which give response to change in blood pressure. Baroreceptors are also called pressoreceptors. Baroreceptors are situated in the carotid sinus and wall of the aorta. Carotid baroreceptors are supplied by Hering nerve, which is the branch of glossopharyngeal nerve. Aortic baroreceptors are supplied by aortic nerve, which is a branch of vagus nerve. Nerve fibers from the baroreceptors reach the nucleus of tractus solitarius, which is situated adjacent to vasomotor center in medulla oblongata.

Role of baroreceptors when blood pressure increases: When arterial blood pressure rises rapidly, baroreceptors are activated and send stimulatory impulses to nucleus of tractus solitarius through glossopharyngeal and vagus nerves. It inhibits the vasoconstrictor area and excites the vasodilator area. Inhibition of vasoconstrictor area reduces vasomotor tone. Reduction in

vasomotor tone causes vasodilatation, resulting in decreased peripheral resistance. Simultaneous excitation of vasodilator center increases vagal tone. This decreases the rate and force of contraction of heart, leading to reduction in cardiac output.

Role of baroreceptors when blood pressure decreases: The fall in arterial blood pressure decreases the pressure in carotid sinus, causing inactivation of baroreceptors. Now, there is no inhibition of vasoconstrictor center or excitation of vasodilator center. Therefore, the blood pressure rises. Since the baroreceptor mechanism acts against the rise in arterial blood pressure, it is called **pressure buffer mechanism** and the nerves from baroreceptors are called the **buffer nerves**.

2. **Chemoreceptor mechanism:** Chemoreceptors are the receptors giving response to change in chemical constituents of blood. Peripheral chemoreceptors are situated in the carotid body and aortic body. Chemoreceptors in the carotid body are supplied by hering nerve, which is the branch of glossopharyngeal nerve. Chemoreceptors in the aortic body are supplied by aortic nerve which is the branch of vagus nerve.

Function: Peripheral chemoreceptors are sensitive to lack of oxygen, excess of carbon dioxide and hydrogen ion concentration in blood. Whenever blood pressure decreases, blood flow to chemoreceptors decreases, resulting in decreased oxygen content and excess of carbon dioxide and hydrogen ion. These factors excite the chemoreceptors, which send impulses to stimulate vasoconstrictor center. Blood pressure rises and blood flow increases.

Sinoaortic mechanism: Mechanism of action of baroreceptors and chemoreceptors in carotid and aortic region constitute sinoaortic mechanism. Nerves supplying the baroreceptors and chemoreceptors are called **buffer nerves** because these nerves regulate the heart rate, blood pressure and respiration.

3. **Higher centers:** Vasomotor center is also controlled by the impulses from the two higher centers in the brain.

- i. **Cerebral cortex:** During emotional disturbances, Area 13 in cerebral cortex sends impulses to vasomotor center. Vasomotor center is activated, the vasomotor tone is increased and the pressure rises.
- ii. **Hypothalamus:** Stimulation of posterior and lateral nuclei of hypothalamus causes vasoconstriction and increase in blood pressure. Stimulation of preoptic area causes vasodilatation and decrease in blood pressure.

4. **Respiratory centers:** During the beginning of expiration, arterial blood pressure increases slightly, i.e. by 4–6 mm Hg. It decreases during later part of expiration and during inspiration.

II. Renal Mechanism for Regulation of Blood Pressure: Long-term Regulation

Kidneys regulate arterial blood pressure by two ways:

1. **By regulation of extracellular fluid volume:** When the blood pressure increases, kidneys excrete large amounts of water and salt, by means of pressure diuresis and pressure natriuresis. This leads to decrease in ECF volume and blood volume.
2. **Through renin-angiotensin mechanism:** When blood pressure and ECF volume decrease, renin secretion from kidneys is increased. It converts angiotensinogen into angiotensin I. This is converted into angiotensin II by ACE (angiotensin converting enzyme). Angiotensin II causes constriction of arterioles in the body, so that the peripheral resistance is increased and blood pressure rises. It causes constriction of afferent arterioles in kidneys, so that glomerular filtration reduces. This results in retention of water and salts, increases ECF volume to normal level. Simultaneously, angiotensin II stimulates the adrenal cortex to secrete aldosterone. This hormone increases reabsorption of sodium from renal tubules. Sodium reabsorption is followed by water reabsorption, resulting in increased ECF volume and blood volume.

III. Hormonal Mechanism for Regulation of Blood Pressure

Hormones which increase blood pressure

1. Adrenaline
2. Noradrenaline
3. Thyroxine
4. Aldosterone
5. Vasopressin
6. Angiotensin II, III and IV
7. Serotonin

Hormones which decrease blood pressure

1. Vasoactive intestinal polypeptide
2. Bradykinin
3. Prostaglandins
4. Histamine
5. Acetylcholine
6. Atrial natriuretic peptide
7. Brain natriuretic peptide
8. C-type natriuretic peptide

IV. Local Mechanism for Regulation of Blood Pressure

1. **Local vasoconstrictors:** These substances are called endothelium-derived constricting factors (EDCF). Common EDCF are endothelins (ET)-ET1, ET2 and ET3.
2. **Local vasodilators:** Local vasodilators are of two types:
 - a. *Vasodilators of metabolic origin:* Carbon dioxide, lactate, hydrogen ions and adenosine.
 - b. *Vasodilators of endothelial origin:* Nitric oxide.

Q. 7. Write a note on hypertension.

(RGUHS, Nov. 2011)

Ans. Hypertension is defined as the persistent high blood pressure. Clinically, when the systolic pressure remains elevated above 150 mm Hg and diastolic pressure remains elevated above 90 mm Hg, it is considered as hypertension. If there is increase only in systolic pressure, it is called **systolic hypertension**.

Types of Hypertension

Hypertension is divided into two types:

1. **Primary hypertension or essential hypertension:** Primary hypertension is the elevated blood pressure in the absence of any underlying disease. Arterial blood pressure is increased because of increased peripheral resistance, which occurs due to some unknown cause. Primary hypertension is of two types:
 - i. Benign hypertension
 - ii. Malignant hypertension
2. **Secondary hypertension:** Secondary hypertension is the high blood pressure due to some underlying disorders. The different forms of secondary hypertension are:
 - i. Cardiovascular hypertension
 - ii. Endocrine hypertension
 - iii. Renal hypertension
 - iv. Neurogenic hypertension
 - v. Hypertension during pregnancy

Some pregnant women develop hypertension because of **toxemia of pregnancy**. Arterial blood pressure is elevated by the low glomerular filtration rate and retention of sodium and water. It may be because of some autoimmune processes during pregnancy or release of some vasoconstrictor agents from placenta or due to the excessive secretion of hormones causing rise in blood pressure. Hypertension is associated with **convulsions in eclampsia**.

Q. 8. Write a note on central venous pressure.

Ans. Venous pressure is the pressure exerted by the contained blood in the veins. The pressure in vena cava

and right atrium is called **central venous pressure**. The pressure in peripheral veins is called **peripheral venous pressure**. Pressure is not same in all the veins.

Venous pressure in extremities of the body: Venous pressure is less in the parts of the body above the level of the heart and it is more in parts below the level of the heart.

Venous pressure in central and peripheral veins: Pressure is greater in peripheral veins than in central veins.

Variations of venous pressure: Venous pressure is altered both in physiological and pathological conditions.

Physiological variations: Venous pressure increases in:

1. Changing from standing to supine position
2. Tilting the body
3. Forced expiration (Valsalva maneuver)
4. Contraction of abdominal and limb muscles
5. Effect of gravity during prolonged traveling or standing
6. Excitement

Pathological variations: Venous pressure increases in:

1. Low cardiac output
2. Congestive heart failure
3. Venous obstruction
4. Failure of valves in veins
5. Paralysis of muscles
6. Immobilization of parts of body
7. Renal failure

Venous pressure decreases in: (i) Severe hemorrhage, (ii) surgical shock.

Q. 9. Write a short note on heart sounds.

(TNMGR, Oct. 1999)

Ans. Heart sounds are the sounds produced by mechanical activities of heart during each cardiac cycle. Heart sounds are produced by:

1. Flow of blood through cardiac chambers
2. Contraction of cardiac muscle
3. Closure of valves of the heart

Importance of heart sounds: Alteration in the heart sounds indicates cardiac diseases involving valves of the heart.

First heart sound: First heart sound is produced during isometric contraction period and earlier part of ejection period.

Causes

1. **Valvular factor:** Synchronous closure of atrio-ventricular valves.

2. **Vascular factor:** Rush of blood from the ventricles into aorta and pulmonary artery during ejection period.
3. **Muscular factor:** Myocardial tension and the contraction of ventricular muscle.
4. **Atrial factor:** Vibrations produced by the atrial systole.

Characteristics: First heart sound is a long, soft and low-pitched sound. It resembles the spoken word 'LUBB'. The duration of this sound is 0.10 to 0.17 second.

Applied Physiology

1. **Reduplication of first heart sound:** Reduplication means splitting of the heart sound. First heart sound is split when the atrioventricular valves do not close simultaneously (asynchronous closure). It occurs in stenosis of atrioventricular valves and atrial septal defect.
2. **Soft first heart sound:** A soft first heart sound is heard in low blood pressure, severe heart failure, myocardial infarction and myxedema.
3. **Loud or accentuated first heart sound:** Mitral stenosis, Wolff-Parkinson-White syndrome and acute rheumatic fever.
4. **Cannon sound:** Cannon sound refers to the loud first heart sound that is heard intermittently. It is heard in ventricular tachycardia and complete atrio-ventricular block.

First heart sound and ECG: First heart sound coincides with peak of 'R' wave in ECG.

Second heart sound: Second heart sound is produced at the end of protodiastolic period.

Cause: Second heart sound is produced due to the sudden and synchronous closure of the semilunar valves.

Characteristics: Second heart sound is a short, sharp and high-pitched sound. It resembles the spoken word 'DUBB' (or DUP). Duration of second heart sound is 0.10 to 0.14 second.

Applied Physiology

1. **Reduplication of second heart sound:** Due to asynchronous closure of semilunar valves. It occurs during deep inspiration, pulmonary stenosis, right bundle branch block and right ventricular hypertrophy.
2. **Loud or accentuated second heart sound:** During systemic hypertension and coarctation (narrowing) of aorta, pulmonary hypertension.
3. **Soft second heart sound:** In heart failure.

Second heart sound and ECG: Second heart sound coincides with the 'T' wave in ECG. Sometimes, it may precede the 'T' wave or it may commence after the peak of 'T' wave.

Third heart sound: Third heart sound is a low-pitched sound that is produced during rapid filling period of the cardiac cycle. It is also called **ventricular gallop** or **protodiastolic gallop**, as it is produced during earlier part of diastole. Usually, the third heart sound is inaudible by stethoscope and it can be heard only by using microphone.

Causes: Third heart sound is produced by the rushing of blood into ventricles and vibrations set up in the ventricular wall during rapid filling phase.

Characteristics: Third heart sound is a short- and low-pitched sound. Duration of this sound is 0.07 to 0.10 second.

Conditions when third heart sound becomes audible by stethoscope: In children and athletes, aortic regurgitation, cardiac failure and cardiomyopathy with dilated ventricles. When third heart sound is heard by stethoscope, the condition is called **triple heart sound**.

Third heart sound and ECG: Third heart sound appears between 'T' and 'P' waves of ECG.

Fourth heart sound: Normally, the fourth heart sound is an inaudible sound. It becomes audible only in pathological conditions. It is studied only by graphical recording, i.e. by phonocardiography. This sound is produced during atrial systole (late diastole) and it is considered as the physiologic atrial sound. It is also called **atrial gallop** or **presystolic gallop**.

Causes: Fourth heart sound is produced by contraction of atrial musculature and vibrations are set up in atrial musculature, flaps of the atrioventricular valves during systole.

Characteristics: Fourth heart sound is a short- and low-pitched sound. Duration of this sound is 0.02 to 0.04 second.

Conditions when fourth heart sound becomes audible: Ventricular hypertrophy, long-standing hypertension and aortic stenosis. When fourth heart sound is heard by stethoscope, the condition is called triple heart sound.

Fourth heart sound and ECG: Fourth heart sound coincides with the interval between the end of 'P' wave and the onset of 'Q' wave.

Q. 10. Write a short note on cyanosis. (HP, May 2012)

Ans. Cyanosis is defined as the diffused bluish coloration of skin and mucous membrane. It is due to the presence of large amount of reduced hemoglobin in the blood. Quantity of reduced hemoglobin should be at least 5 to 7 g/dl in the blood to cause cyanosis.

Distribution of Cyanosis

When it occurs, cyanosis is distributed all over the body. But, it is more marked in certain regions where the skin is thin. These areas are lips, cheeks, ear lobes, nose and fingertips above the base of the nail.

Conditions

1. Arterial hypoxia and stagnant hypoxia
2. Poisoning
3. Polycythemia

Cyanosis and Anemia

Cyanosis usually occurs only when the quantity of reduced hemoglobin is about 5 to 7 g/dl. But, in anemia, the hemoglobin content itself is less. So, cyanosis cannot occur in anemia.

4. RESPIRATORY SYSTEM

Q. 1. Write about mechanism of respiration.

Ans. Respiration occurs in two phases, namely inspiration and expiration. During inspiration, thoracic cage enlarges and lungs expand so that air enters the lungs easily. During expiration, the thoracic cage and lungs decrease in size and attain the preinspiratory position so that air leaves the lungs easily. During normal quiet breathing, inspiration is the **active process** and expiration is the **passive process**.

Muscles of Respiration

- a. **Inspiratory muscles:** Primary inspiratory muscles are the diaphragm, and external intercostal muscles. Sternocleidomastoid, scalene, anterior serrati, elevators of scapulae and pectorals are the accessory inspiratory muscles.
- b. **Expiratory muscles:** Primary expiratory muscles are the internal intercostal muscles. Accessory expiratory muscles are the abdominal muscles.

Movements of Thoracic Cage

Inspiration causes enlargement of thoracic cage. Anteroposterior and transverse diameters of thoracic cage are increased by the elevation of ribs. Vertical diameter is increased by the descent of diaphragm. In

general, change in the size of thoracic cavity occurs because of the movements of four units of structures:

1. **Thoracic lid:** Formed by manubrium sterni and the first pair of ribs. It is also called **thoracic operculum**. Movement of thoracic lid increases the **anteroposterior diameter** of thoracic cage.
2. **Upper costal series:** Formed by second to sixth pair of ribs. Movement of upper costal series increases the **anteroposterior** and **transverse diameter** of the thoracic cage.
Movement of upper costal series is of two types
 - i. Pump handle movement
 - ii. Bucket handle movement.
3. **Lower costal series:** Formed by seventh to tenth pair of ribs. Movement of lower costal series increases the **transverse diameter** of thoracic cage by bucket handle movement.
4. **Diaphragm:** Movement of diaphragm increases the vertical diameter of thoracic cage.

Movements of Lungs

During inspiration, due to the enlargement of thoracic cage, the negative pressure is increased in the thoracic cavity. It causes expansion of the lungs. During expiration, the thoracic cavity decreases in size to the **preinspiratory position**. Pressure in the thoracic cage also comes back to the preinspiratory level. It compresses the lung tissues so that, the air is expelled out of lungs.

Q. 2. Write a note on respiratory centers.

(TNMGR, Oct. 1999; Feb. 2005)

Q. Write a note on neural control of respiration.

(TNMGR, April 1997)

Ans. Respiratory centers are group of neurons, which control the rate, rhythm and force of respiration. These centers are bilaterally situated in reticular formation of the brainstem. Depending upon the situation in brainstem, the respiratory centers are classified into two groups.

A. Medullary Centers

1. **Dorsal respiratory group of neurons:** Dorsal respiratory group of neurons are diffusely situated in the nucleus of **tractus solitarius** which is present in the upper part of the medulla oblongata. All the neurons of dorsal respiratory group are **inspiratory neurons** and generate **inspiratory ramp** by the virtue of their **autorhythmic property**.

Function: Dorsal group of neurons are responsible for basic rhythm of respiration.

2. **Ventral respiratory group of neurons:** Ventral respiratory group of neurons are present in **nucleus ambiguus** and **nucleus retroambiguus**. These two nuclei are situated in the medulla oblongata, anterior and lateral to the nucleus of tractus solitarius. Ventral respiratory group has both **inspiratory** and **expiratory neurons**. Inspiratory neurons are found in the central area of the group. Expiratory neurons are in the caudal and rostral areas of the group.

Function: Normally, ventral group neurons are inactive during quiet breathing and become active during forced breathing. During forced breathing, these neurons stimulate both inspiratory muscles and expiratory muscles.

B. Pontine Centers

1. **Apneustic center:** Apneustic center is situated in the reticular formation of lower pons.

Function: Apneustic center increases depth of inspiration by acting directly on dorsal group neurons.

Apneusis is an abnormal pattern of respiration, characterized by prolonged inspiration followed by short, inefficient expiration.

2. **Pneumotaxic center:** Pneumotaxic center is situated in the dorsolateral part of **reticular formation** in **upper pons**. It is formed by neurons of medial **parabrachial** and **subparabrachial nuclei**. Subparabrachial nucleus is also called **ventral parabrachial** or **Kölliker-Fuse nucleus**.

Function: Primary function of pneumotaxic center is to control the medullary respiratory centers, particularly the dorsal group neurons.

Connections of Respiratory Centers

Efferent pathway: Nerve fibers from respiratory centers leave the brainstem and descend in anterior part of lateral columns of spinal cord. These nerve fibers terminate on motor neurons in the anterior horn cells of cervical and thoracic segments of spinal cord. From motor neurons of spinal cord, two sets of nerve fibers arise:

1. Phrenic nerve fibers (C3 to C5), which supply the diaphragm.
2. Intercostal nerve fibers (T1 to T11), which supply the external intercostal muscles.
Vagus nerve also contains some efferent fibers from the respiratory centers.

Afferent pathway: Respiratory centers receive afferent impulses from:

1. Peripheral chemoreceptors and baroreceptors via branches of glossopharyngeal and vagus nerves.

2. Stretch receptors of lungs via vagus nerve.

By receiving afferent impulses from these receptors, respiratory centers modulate the movements of thoracic cage and lungs through efferent nerve fibers.

Factors Affecting Respiratory Centers

Respiratory centers regulate the respiratory movements by receiving impulses from various sources in the body.

1. **Impulses from higher centers:** Higher centers alter the respiration by sending impulses directly to dorsal group of neurons. Impulses from anterior cingulate gyrus, genu of corpus callosum, olfactory tubercle and posterior orbital gyrus of cerebral cortex inhibit respiration. Impulses from motor area and sylvian area of cerebral cortex cause **forced breathing**.

2. Impulses from stretch receptors of lungs

Hering-Breuer reflex: Hering-Breuer reflex is a **protective reflex** that restricts inspiration and prevents overstretching of lung tissues. It is initiated by the stimulation of stretch receptors of air passage. Expansion of lungs during inspiration stimulates the stretch receptors. Impulses from stretch receptors reach the dorsal group neurons via vagal afferent fibers and inhibit them. The above mentioned reflex is called **Hering-Breuer inflation reflex** since it restricts the inspiration limits the overstretching of lung tissues. Reverse of this reflex is called **Hering-Breuer deflation reflex** and it takes place during expiration. During expiration, as the stretching of lungs is absent, deflation occurs.

3. **Impulses from 'J' receptors of lungs:** 'J' receptors are **juxta-capillary receptors** which are present on the wall of the alveoli and have close contact with the pulmonary capillaries. These receptors are the sensory nerve endings of vagus. Nerve fibers from these receptors are nonmyelinated and belong to C type. Conditions when 'J' receptors are stimulated (i) pulmonary congestion, (ii) pulmonary edema, (iii) pneumonia, (iv) over inflation of lungs, (v) micro-embolism in pulmonary capillaries, and (vi) stimulation by exogenous and endogenous chemical substances. **Effect of stimulation of 'J' receptors:** Stimulation of the 'J' receptors produces a reflex response, which is characterized by **apnea**. Apnea is followed by hyperventilation, bradycardia, hypotension and weakness of skeletal muscles. These receptors are responsible for hyperventilation in patients affected by pulmonary congestion and left heart failure.

4. **Impulses from irritant receptors of lungs:** Irritant receptors are stimulated by irritant chemical agents such as ammonia and sulfur dioxide. These receptors send afferent impulses to respiratory centers via

vagal nerve fibers. Stimulation of irritant receptors produces **reflex hyperventilation** along with **bronchospasm** prevents further entry of harmful agents into the alveoli.

5. **Impulses from baroreceptors:** Whenever arterial blood pressure increases, baroreceptors are activated and send inhibitory impulses to vasomotor center in medulla oblongata. This causes decrease in blood pressure and inhibition of respiration.

6. **Impulses from chemoreceptors:** Chemoreceptors play an important role in the chemical regulation of respiration.

7. **Impulses from proprioceptors:** Proprioceptors are the receptors which give response to change in the position of body. These receptors are situated in joints, tendons and muscles. Proprioceptors are stimulated during the muscular exercise and send impulses to brain, particularly cerebral cortex, through somatic afferent nerves. Cerebral cortex, in turn causes hyperventilation by sending impulses to medullary respiratory centers.

8. **Impulses from thermoreceptors:** Thermoreceptors are cutaneous receptors, which give response to change in the environmental temperature. Thermoreceptors are of two types, namely receptors for cold and receptors for warmth. When body is exposed to cold, cold receptors are stimulated and send impulses to cerebral cortex via somatic afferent nerves. Cerebral cortex in turn, stimulates the respiratory centers and causes hyperventilation.

9. **Impulses from pain receptors:** Whenever pain receptors are stimulated, the impulses are sent to cerebral cortex via somatic afferent nerves. Cerebral cortex, in turn, stimulates the respiratory centers and causes hyperventilation.

Q. 3. Write a short note on chemical control of respiration. (TNMGR, Sept. 2008)

Ans. Chemical mechanism of regulation of respiration is operated through the chemoreceptors. Chemoreceptors are the sensory nerve endings, which give response to changes in chemical constituents of blood.

Changes in chemical constituents of blood which stimulate chemoreceptors

1. Hypoxia (decreased pO_2)
2. Hypercapnia (increased pCO_2)
3. Increased hydrogen ion concentration

Types of chemoreceptors: Chemoreceptors are classified into two groups:

1. Central chemoreceptors
2. Peripheral chemoreceptors

Central chemoreceptors: Central chemoreceptors are situated in deeper part of medulla oblongata. This area is known as **chemosensitive area** and the neurons are called **chemoreceptors**. Central chemoreceptors are connected with respiratory centers, particularly the dorsal respiratory group of neurons through synapses. As carbon dioxide increases in the blood, it can easily cross the blood–brain barrier and blood cerebrospinal fluid barrier and enter the interstitial fluid of brain or the cerebrospinal fluid. There, the carbon dioxide combines with water to form carbonic acid. Since carbonic acid is unstable, it immediately dissociates into hydrogen ion and bicarbonate ion. Hydrogen ions stimulate the central chemoreceptors. From chemoreceptors, the excitatory impulses are sent to dorsal respiratory group of neurons, resulting in increased ventilation (increased rate and force of breathing).

Peripheral chemoreceptors: Peripheral chemoreceptors are the chemoreceptors present in carotid and aortic region. Hypoxia is the most potent stimulant for peripheral chemoreceptors. Hypoxia causes closure of oxygen sensitive potassium channels and prevents potassium efflux. This leads to depolarization of **glomus cells** (receptor potential) and generation of action potentials in nerve ending. These impulses pass through aortic and Hering nerves and excite the dorsal group of neurons. Dorsal group of neurons, in turn, send excitatory impulses to respiratory muscles, resulting in increased ventilation.

Q. 4. Write a short note on hypoxia.

Ans. Hypoxia is defined as reduced availability of oxygen to the tissues.

Classification

1. **Hypoxic hypoxia:** Hypoxic hypoxia means decreased oxygen content in blood. It is also called arterial hypoxia.

Causes

- i. Low oxygen tension in inspired air—high altitude.
 - ii. Respiratory disorders—asthma, emphysema, and pneumothorax.
 - iii. Cardiac disorders—congestive heart failure.
2. **Anemic hypoxia:** Characterized by the inability of blood to carry enough amount of oxygen.

Causes

- i. Decreased number of RBCs.
- ii. Decreased hemoglobin content in the blood.
- iii. Formation of altered hemoglobin.

- iv. Combination of hemoglobin with gases other than oxygen and carbon dioxide.

3. **Stagnant hypoxia:** Stagnant hypoxia is the hypoxia caused by decreased velocity of blood flow. It is otherwise called hypokinetic hypoxia.

Causes: Congestive cardiac failure, hemorrhage, surgical shock, and thrombosis.

4. **Histotoxic hypoxia:** Due the inability of tissues to utilize oxygen. For example, cyanide or sulfide poisoning.

Effects of Hypoxia

Immediate effects: Induces secretion of **erythropoietin** from kidney. Initially, increase in rate and force of contraction of heart, cardiac output and blood pressure. Later, there is reduction in the rate and force of contraction of heart. Cardiac output and blood pressure are also decreased. Initially, respiratory rate increases due to chemoreceptor reflex. Later, the respiration tends to be **shallow and periodic**. Finally, the rate and force of breathing are reduced to a great extent due to the failure of respiratory centers. Hypoxia is associated with loss of appetite, nausea and vomiting. Mouth becomes dry and there is a feeling of thirst. **Alkaline urine** is excreted. Individual is depressed, apathetic with general loss of self control. The person becomes talkative, quarrelsome, ill-tempered and rude, loss of consciousness, **coma, and leads to death**.

Delayed effects of hypoxia: Person becomes highly irritable and develops the symptoms of mountain sickness, such as nausea, vomiting, depression, weakness and fatigue.

Treatment for hypoxia: Oxygen therapy.

Q. 5. Discuss in detail the causes, prevention and management of acute respiratory distress syndrome.

(TNMGR, April 2012)

Ans. Acute respiratory distress syndrome (ARDS) is clinical syndrome categorized by progressive hypoxemia, dyspnea, and increased work of breathing that is unresponsive to standard respiratory therapy. It is an acute, diffuse pulmonary inflammatory response to either direct or indirect blood-borne insults that originates from extrapulmonary pathology. The criteria defining ARDS are:

- i. Hypoxemia.
- ii. Chest radiograph showing diffuse bilateral infiltrates.
- iii. Absence of a raised left atrial pressure.
- iv. Impaired lung compliance.

Causes

A. Inhalational (Direct)

1. Aspiration of gastric contents
2. Toxic gases
3. Pneumonia
4. Blunt chest trauma

B. Blood-borne (Indirect)

1. Sepsis
2. Necrotic tissue
3. Multiple trauma
4. Severe burns
5. Major blood transfusion reaction
6. Anaphylaxis
7. Fat embolism
8. Carcinomatosis

Prevention of ARDS can be accomplished by preventing the infections and injuries that cause it. Even if trauma or infection cannot be prevented, early aggressive treatment may avert ARDS. Promptly hydrating persons in shock or administering antibiotics to persons with pneumonia may correct the underlying process enough to prevent ARDS from developing.

Management

1. **Corticosteroids:** Methylprednisolone (1 mg/kg/day).
2. **Neuromuscular blocking agents:** Cisatracurium (bolus: 0.1–0.2 mg/kg; continuous: 0.5–10 µg/kg/minute).
3. **Inhaled vasodilators:** Nitric oxide (5–20 ppm).
4. **Exogenous surfactant replacement:** Beractant (100 mg/kg).
5. **β₂-adrenergic agonists:** Salbutamol (15 µg/kg/hour).
6. **Anti-inflammatory agents:** Ketokonazole (200–400 mg).
7. **Antioxidants:** N-acetylcysteine (1–10 ml of 20% every 2–6 h).

Q. 6. Write a short note on artificial respiration.

(TNMGR, April 1995, 1998, 2003; March 2007)

Ans. Artificial respiration is required whenever there is an arrest of breathing, without cardiac failure.

Stoppage of oxygen supply for 5 minutes causes irreversible changes in tissues of brain. Purpose of artificial respiration is to ventilate the alveoli and to stimulate the respiratory centers.

Methods of Artificial Respiration

- a. **Manual methods:** Manual methods are of two types:
 1. **Mouth-to-mouth method:** The subject is kept in supine position and the resuscitator (person who

give resuscitation) kneels at the side of the subject. By keeping the thumb on subject's mouth, the lower jaw is pulled downwards. Nostrils of the subject are closed with thumb and index finger of the other hand. Resuscitator then takes a deep breath and exhales into the subject's mouth forcefully. Now, a passive expiration occurs in the subject due to elastic recoil of the lungs. This procedure is repeated at a rate of 12–14 times a minute, till normal respiration is restored. Mouth-to-mouth method is the most effective manual method because, carbon dioxide in expired air of the resuscitator can directly stimulate the respiratory centers and facilitates the onset of respiration. Only disadvantage is that the close contact between the mouths of resuscitator and subject may not be acceptable for various reasons.

2. **Holger Nielsen method or back pressure arm lift method:** Subject is placed in prone position with head turned to one side. Hands are placed under the cheeks with flexion at elbow joint and abduction of arms at the shoulders. Resuscitator kneels beside the head of the subject. By placing the palm of the hands over the back of the subject, the resuscitator bends forward with straight arms (without flexion at elbow) and applies pressure on the back of the subject. Weight of the resuscitator and pressure on back of the subject compresses his chest and expels air from the lungs. Later, the resuscitator leans back. At the same time, he draws the subject's arm forward by holding it just above elbow. The movements are repeated at the rate of 12 per minute, till the normal respiration is restored.

- b. **Mechanical methods:** Mechanical methods of artificial respiration become necessary when the subject needs artificial respiration for long periods. Mechanical methods are of two types:

1. **Drinker method:** The machine used in this method is called iron lung chamber or tank respirator. By using tank respirator, the patient can survive for a longer time, even up to the period of one year till the natural respiratory functions are restored.
2. **Ventilation method:** Apparatus used for ventilation is called ventilator and it is mostly used to treat acute respiratory failure. Ventilator is of two types:
 - a. Volume ventilator
 - b. Pressure ventilator.

Q. 7. Write a short note on cough reflex.

(TNMGR, Nov. 2001)

Ans. Cough is a modified respiratory process characterized by forced expiration.

Causes: Cough is produced mainly by irritant agents. It is also produced by several disorders such as cardiac disorders (congestive heart failure), pulmonary disorders (chronic obstructive pulmonary disease—COPD) and tumor in thorax, which may exert pressure on larynx, trachea, bronchi or lungs.

Mechanism: Cough begins with deep inspiration followed by forced expiration with closed glottis. This increases the intrapleural pressure above 100 mm Hg. Then, glottis opens suddenly with explosive outflow of air at a high velocity. Velocity of the airflow may reach 960 km/hour. It causes expulsion of irritant substances out of the respiratory tract.

Reflex pathway: Receptors that initiate the cough are situated in several locations such as nose, paranasal sinuses, larynx, pharynx, trachea, bronchi, pleura, diaphragm, pericardium, stomach, external auditory canal and tympanic membrane. Afferent nerve fibers pass via vagus, trigeminal, glossopharyngeal and phrenic nerves. The center for cough reflex is in the medulla oblongata. Efferent nerve fibers arising from the medullary center pass through the vagus, phrenic and spinal motor nerves. These nerve fibers activate the primary and accessory respiratory muscles.

5. ENDOCRINE SYSTEM

Q. 1. Describe briefly the importance of endocrine system. (Bangalore Uni., Jan. 1992)

Q. Discuss in detail the endocrinal system of human body. Why is pituitary gland called as ring-master? Add a note on role of parathyroid gland on oral structures and oral health.

(TNMGR, March 2009; PAHER, May 2014)

Q. Discuss the role of pituitary gland in regulation of body functions. (RGUHS, Nov. 2011)

Ans. Endocrine system functions by secreting some chemical substances called **hormones**. Chemical messengers are the substances involved in cell signaling. Chemical messengers are classified into four types:

1. **Endocrine messengers (classical hormones):** A hormone is defined as a chemical messenger, synthesized by endocrine glands and transported by blood to the target organs or tissues. For example, growth hormone and insulin.
2. **Paracrine messengers:** Paracrine messengers are the chemical messengers, which diffuse from the control cells to the target cells through the interstitial fluid. For example, prostaglandins and histamine.

3. **Autocrine messengers:** Autocrine messengers are the chemical messengers that control the source cells which secrete them. For example, leukotrienes.
4. **Neurocrine or neural messengers:** Neurotransmitters and neurohormones. For example, acetylcholine and dopamine.

Endocrine glands: Endocrine glands are the glands which synthesize and release the classical hormones into the blood. Endocrine glands are also called **ductless glands**.

Major Endocrine Glands of the Body

a. Pituitary gland

1. **Anterior pituitary**
 - i. Growth hormone (GH)
 - ii. Thyroid-stimulating hormone (TSH)
 - iii. Adrenocorticotrophic hormone (ACTH)
 - iv. Follicle-stimulating hormone (FSH)
 - v. Luteinizing hormone (LH)
 - vi. Prolactin

2. Posterior pituitary

- i. Antidiuretic hormone (ADH)
- ii. Oxytocin

b. Thyroid gland

- i. Thyroxine (T4)
- ii. Triiodothyronine (T3)
- iii. Calcitonin

c. Parathyroid gland: Parathormone.

d. Pancreas

- i. Insulin
- ii. Glucagon
- iii. Somatostatin
- iv. Pancreatic polypeptide

e. Adrenal gland

1. Adrenal cortex

- i. **Mineralocorticoids:** Aldosterone, 11-deoxycorticosterone
- ii. **Glucocorticoids:** Cortisol, corticosterone
- iii. **Sex hormones:** Androgens, estrogen, progesterone

2. Adrenal medulla

- i. Catecholamines
- ii. Adrenaline (epinephrine)
- iii. Noradrenalin (norepinephrine)
- iv. Dopamine

Pituitary gland or hypophysis is a small endocrine gland with a diameter of 1 cm and weight of 0.5 to 1 g. It is situated in a depression called 'sella turcica', present in the sphenoid bone at the base of skull. It is connected with the hypothalamus by the pituitary stalk or hypophyseal stalk.

Pituitary gland is divided into two divisions:

1. Anterior pituitary or adenohypophysis: **Ectodermal** in origin.
2. Posterior pituitary or neurohypophysis: **Neuroectodermal** in origin.

Hormones Secreted by Anterior Pituitary

1. *Growth hormone (GH) or somatotrophic hormone (STH)*

Actions: GH is responsible for the general growth of the body. Hypersecretion of GH causes enormous growth of the body, leading to gigantism. Deficiency of GH in children causes stunted growth, leading to dwarfism. It increases the size and number of cells by mitotic division. GH also causes specific differentiation of certain types of cells like bone cells and muscle cells. GH also acts on the metabolism of all the three major types of foodstuffs in the body, viz. proteins, lipids and carbohydrates.

- a. *On metabolism:* GH increases the synthesis of proteins, mobilization of lipids and conservation of carbohydrates.
 - b. *On bones:* In embryonic stage, GH is responsible for the differentiation and development of bone cells. In later stages, GH increases the growth of the skeleton. It increases both the length as well as the thickness of the bones.
- #### 2. *Thyroid-stimulating hormone (TSH) or thyrotrophic hormone:* TSH is necessary for the growth and secretory activity of the thyroid gland.
- a. *To increase basal metabolic rate:* Thyroxine increases the metabolic activities in most of the body tissues, except brain, retina, spleen, testes and lungs. It increases BMR by increasing the oxygen consumption of the tissues.
 - b. To help the growth of children.
- #### 3. *Adrenocorticotrophic hormone (ACTH)*
- a. *Functions of mineralocorticoids:* 90% of mineralocorticoids activity is provided by aldosterone. Aldosterone is very essential for life and it maintains the osmolarity and volume of ECF. It is usually called **life-saving hormone** because its absence causes death within 3 days to 2 weeks. Aldosterone has three important functions. It increases:
 1. Reabsorption of sodium from renal tubules.
 2. Excretion of potassium through renal tubules.
 3. Secretion of hydrogen into renal tubules.
 - b. *Functions of glucocorticoids:* Cortisol or hydrocortisone is more potent and it has 95% of glucocorticoid activity. Cortisol is a life-protecting hormone because it helps to withstand the stress and

trauma in life. Glucocorticoids have metabolic effects on carbohydrates, proteins, fats and water. These hormones also show mild mineralocorticoid effect.

4. *Follicle-stimulating hormone (FSH)*

Actions: In males, FSH acts along with testosterone and accelerates the process of spermatogenesis. In females FSH:

1. Causes the secretion of estrogen.
2. Promotes conversion of androgens into estrogen.

5. *Luteinizing hormone (LH)*

Actions: In males, LH stimulates the interstitial cells of Leydig in testes. This hormone is essential for the secretion of testosterone from Leydig cells. In females, LH is:

1. Responsible for ovulation.
2. Necessary for the formation of corpus luteum.
3. Activates the secretory functions of corpus luteum.

6. *Prolactin:* Prolactin is necessary for the final preparation of mammary glands for the production and secretion of milk. Prolactin acts directly on the epithelial cells of mammary glands and causes localized alveolar hyperplasia.

Hormones Secreted by Posterior Pituitary

1. *Antidiuretic hormone (ADH):* Antidiuretic hormone (ADH) is secreted mainly by supraoptic nucleus of hypothalamus. From here, this hormone is transported to posterior pituitary through the nerve fibers of hypothalamo hypophyseal tract, by means of axonic flow.

Actions

1. Retention of water
 2. Vasopressor action
- #### 2. *Oxytocin:* In females, oxytocin acts on mammary glands and uterus. Oxytocin causes ejection of milk from the mammary glands. The process by which the milk is ejected from alveoli of mammary glands is called milk ejection reflex or milk letdown reflex. Oxytocin acts on pregnant uterus and also non-pregnant uterus. Oxytocin causes contraction of uterus and helps in the expulsion of fetus. Oxytocin also stimulates the release of prostaglandins in the placenta. Prostaglandins intensify the uterine contraction induced by oxytocin. The action of oxytocin on non-pregnant uterus is to facilitate the transport of sperms through female genital tract up to the fallopian tube, by producing the uterine contraction during sexual intercourse. In males, the release of oxytocin increases during ejaculation. It facilitates release of sperm into urethra by causing

contraction of smooth muscle fibers in reproductive tract, particularly vas deferens.

Parathyroid gland: Each parathyroid gland is made up of chief cells and oxyphil cells. Chief cells secrete parathormone. Oxyphil cells are the degenerated chief cells. Parathormone (PTH) secreted by parathyroid gland is essential for the maintenance of blood calcium level within a very narrow critical level.

Actions

- a. **On blood calcium level:** Primary action of PTH is to maintain the blood calcium level within the critical range of 9 to 11 mg/dl. PTH maintains blood calcium level by acting on:
 1. **Bone:** Parathormone enhances the resorption of calcium from the bones.
 2. **Kidney:** PTH increases the reabsorption of calcium from the renal tubules along with magnesium ions and hydrogen ions. PTH also increases the formation of 1, 25-dihydroxycholecalciferol (activated form of vitamin D) from 25-hydroxycholecalciferol in kidneys.
 3. **Gastrointestinal tract:** PTH increases the absorption of calcium ions from the GI tract indirectly, by increasing the formation of 1, 25-dihydroxycholecalciferol in the kidneys.
- b. **Blood phosphate level:** PTH decreases blood level of phosphate by increasing its urinary excretion. It also acts on bone and GIT.
 1. **Bone:** Along with calcium resorption, PTH also increases phosphate absorption from the bones.
 2. **Kidney:** Phosphaturic action: It is the effect of PTH by which phosphate is excreted through urine.
 3. **Gastrointestinal tract:** Parathormone increases the absorption of phosphate from GIT through calcitriol.

Disorders of Parathyroid Glands

1. **Hypoparathyroidism:** Leads to hypocalcemia, by decreasing the resorption of calcium from bones. Hypocalcemia causes neuromuscular hyperexcitability, resulting in hypocalcemic tetany. Normally, tetany occurs when plasma calcium level falls below 6 mg/dl.
 - a. **Hypocalcemic tetany:** Characterized by violent and painful muscular spasm (spasm = involuntary muscular contraction), particularly in feet and hand. It is because of hyperexcitability of nerves and skeletal muscles due to calcium deficiency. Signs and symptoms of hypocalcemic tetany:
 1. Hyper-reflexia and convulsions
 2. Carpopedal spasm

3. Laryngeal stridor

4. Cardiovascular changes

5. Other features

- i. Decreased permeability of the cell membrane
- ii. Dry skin with brittle nails
- iii. Hair loss
- iv. Grand mal, petit mal or other seizures
- v. Signs of mental retardation in children or dementia in adults.

Latent tetany/subclinical tetany is the neuromuscular hyperexcitability due to hypocalcemia that develops before the onset of tetany. It is characterized by general weakness and cramps in feet and hand. Hyperexcitability in these patients is detected by some signs, which do not appear in normal persons.

1. Trousseau sign
2. Chvostek sign
3. Erb sign also called Erb-Westphal sign

2. **Hyperparathyroidism (TNMGR, March 2007):** It results in hypercalcemia:

1. Primary hyperparathyroidism
2. Secondary hyperparathyroidism
3. Tertiary hyperparathyroidism

Signs and Symptoms of Hypercalcemia

- i. Depression of the nervous system
- ii. Sluggishness of reflex activities
- iii. Reduced ST segment and QT interval in ECG
- iv. Lack of appetite
- v. Constipation
- vi. Development of bone diseases such as osteitis fibrosa cystica
- vii. Development of parathyroid poisoning.

Q. 2. Write a note on growth hormone.

(TNMGR, April 2001; Sept. 2009; April 2013; Oct. 2014)

Ans. Growth hormone is secreted by somatotropes which are the acidophilic cells of anterior pituitary. GH is protein in nature, having a single-chain polypeptide with 191 amino acids. Its molecular weight is 21,500. Basal level of GH concentration in blood of normal adult is up to 300 g/dl and in children, it is up to 500 ng/dl. Its daily output in adults is 0.5 to 1.0 mg.

Transport: Growth hormone is transported in blood by GH-binding proteins (GHBP).

Half-life and metabolism: Half-life of circulating growth hormone is about 20 minutes. It is degraded in liver and kidney.

Actions of Growth Hormone

1. **On metabolism:** GH increases the synthesis of proteins, mobilization of lipids and conservation of carbohydrates.
 - a. **On protein metabolism:** GH accelerates the synthesis of proteins by:
 - i. Increasing amino acid transport through cell membrane.
 - ii. Increasing ribonucleic acid (RNA) translation. Because of this, ribosomes are activated and more proteins are synthesized.
 - iii. Increasing transcription of DNA to RNA. It also stimulates the transcription of DNA to RNA.
 - iv. Decreasing catabolism of protein.
 - v. Promoting anabolism of proteins indirectly.
 - b. **On fat metabolism:** GH mobilizes fats from adipose tissue. So, the concentration of fatty acids increases in the body fluids. These fatty acids are used for the production of energy by the cells. Thus, the proteins are spared.
 - c. **On carbohydrate metabolism:** Major action of GH on carbohydrates is the conservation of glucose.
 - i. Decrease in the **peripheral utilization** of glucose for the production of energy.
 - ii. Increase in the deposition of glycogen in the cells.
 - iii. Decrease in the uptake of glucose by the cells.
 - iv. Diabetogenic effect of GH: Hypersecretion of GH increases blood glucose level enormously.
2. **On bones:** In embryonic stage, GH is responsible for the differentiation and development of bone cells. In later stages, GH increases the growth of the skeleton. In bones, GH increases:
 - i. Synthesis and deposition of proteins by chondrocytes and osteogenic cells.
 - ii. Multiplication of **chondrocytes** and **osteogenic cells** by enhancing the intestinal calcium absorption.
 - iii. Formation of new bones by converting chondrocytes into osteogenic cells.
 - iv. Availability of calcium for mineralization of bone matrix.

GH increases the length of the bones, until epiphysis fuses with shaft, which occurs at the time of puberty. After the **epiphyseal fusion**, length of the bones cannot be increased. However, it stimulates the **osteoblasts** strongly. So, the bone continues to grow in thickness throughout the life. Hypersecretion of GH before the fusion of epiphysis with the shaft of the bones causes enormous growth of the skeleton, leading to a condition called **gigantism**. Hypersecretion of GH after the fusion of epiphysis with the shaft of the bones leads to a condition called **acromegaly**.

Mode of action of GH somatomedin: GH stimulates the liver to secrete somatomedin. Somatomedin is defined as a substance through which growth hormone acts. Somatomedins are of two types:

- i. Insulin-like growth factor-I (IGF-I), which is also called somatomedin C.
- ii. Insulin-like growth factor-II.

Somatomedin C (IGF-I) acts on the bones and protein metabolism. Insulin-like growth factor-II plays an important role in the growth of fetus.

GH receptor is called **growth hormone secretagogue** (GHS) receptor.

Regulation of GH secretion: GH secretion is stimulated by:

1. Hypoglycemia
2. Fasting
3. Starvation
4. Exercise
5. Stress and trauma
6. Initial stages of sleep

GH secretion is inhibited by

1. Hyperglycemia.
2. Increase in free fatty acids in blood.
3. Later stages of sleep.

Hypothalamus regulates GH secretion via three hormones

1. **Growth hormone-releasing hormone (GHRH):** It increases the GH secretion by stimulating the somatotropes of anterior pituitary.
2. **Growth hormone-releasing polypeptide (GHRP):** It increases the release of GHRH from hypothalamus and GH from pituitary.
3. **Growth hormone-inhibitory hormone (GHIH) or somatostatin:** It decreases the GH secretion.

Q. 3. Write a short note on thyroid-stimulating hormone. (TNMGR, April 2012)

Ans. Thyroid-stimulating hormone (TSH) secreted by anterior pituitary is the major factor regulating the synthesis and release of thyroid hormones. It is also necessary for the growth and the secretory activity of the thyroid gland.

Chemistry: Thyroid-stimulating hormone is a peptide hormone with one α -chain and one β -chain.

Half-life and plasma level: Half-life of TSH is about 60 minutes. The normal plasma level of TSH is approximately 2 U/ml.

Actions of thyroid-stimulating hormone: Thyroid-stimulating hormone increases:

1. The number of follicular cells of thyroid.
2. It causes the development of thyroid follicles.
3. Size and secretory activity of follicular cells.
4. Iodide pump and iodide trapping in follicular cells.
5. Thyroglobulin secretion into follicles.
6. Iodination of tyrosine and coupling to form the hormones.
7. Proteolysis of the thyroglobulin.

Mode of action of TSH: TSH acts through cyclic AMP mechanism.

Q. 4. Write about importance of thyroid hormone in growth. (BFUHS, May 2011; HP, 2013; RUHS, May 2015)

Ans. Thyroid hormones have general and specific effects on growth. Increase in thyroxine secretion accelerates the growth of the body, especially in growing children. Lack of thyroxine arrests the growth. At the same time, thyroxine causes early closure of epiphysis. So, the height of the individual may be slightly less in hypothyroidism. Thyroxine is more important to promote growth and development of brain during fetal life and first few years of postnatal life. Deficiency of thyroid hormones during this period leads to mental retardation.

Q. 5. Write a short note on hypothyroidism.

(TNMGR, Oct. 1999; RGUHS, May 2013)

Ans. Decreased secretion of thyroid hormones is called hypothyroidism. Hypothyroidism leads to myxedema in adults and cretinism in children.

Myxedema: Myxedema is the hypothyroidism in adults, characterized by generalized edematous appearance.

Causes: Due to diseases of thyroid gland, genetic disorder or iodine deficiency, deficiency of thyroid-stimulating hormone or thyrotropin-releasing hormone. Common cause of myxedema is the autoimmune disease called **Hashimoto's thyroiditis**, which is common in late middle-aged women.

Signs and symptoms of myxedema: Typical feature of this disorder is an edematous appearance throughout the body. It is associated with the following symptoms:

1. Swelling of the face
2. Bagging under the eyes
3. Non-pitting type of edema
4. Atherosclerosis: **Atherosclerosis** produces **arteriosclerosis**, which refers to thickening and stiffening of arterial wall. Arteriosclerosis causes hypertension.

Other general features of hypothyroidism in adults are

1. Anemia
2. Fatigue and muscular sluggishness

3. Extreme somnolence with sleeping up to 14 to 16 hours per day
4. Menorrhagia and polymenorrhea
5. Decreased cardiovascular functions
6. Increase in body weight
7. Constipation
8. Mental sluggishness
9. Depressed hair growth
10. Scaliness of the skin
11. Frog-like husky voice
12. Cold intolerance.

Cretinism: Cretinism is the hypothyroidism in children, characterized by stunted growth.

Causes: It occurs due to congenital absence of thyroid gland, genetic disorder or lack of iodine in the diet.

Clinical Features

1. A newborn baby with thyroid deficiency may appear normal at the time of birth because thyroxine might have been supplied from mother. But a few weeks after birth, the baby starts developing the signs like sluggish movements and **croaking sound** while crying. Unless treated immediately, the baby will be mentally retarded permanently.
2. Skeletal growth is more affected than the soft tissues. So, there is stunted growth with bloated body. The tongue becomes so big that it hangs down with dripping of saliva. The big tongue obstructs swallowing and breathing. The tongue produces characteristic guttural breathing that may sometimes **choke** the baby.

Q. 6. Write a short note on sex hormones.

(RGUHS, Nov. 2006)

Ans. Adrenal sex hormones are secreted mainly by zona reticularis. Zona fasciculata secretes small quantities of sex hormones. Adrenal cortex secretes mainly the male sex hormones, which are called **androgens**. But small quantity of **estrogen** and **progesterone** are also secreted by adrenal cortex. Androgens secreted by adrenal cortex:

1. Dehydroepiandrosterone
2. Androstenedione
3. Testosterone

Dehydroepiandrosterone is the most active adrenal androgen. Androgens, in general, are responsible for masculine features of the body. But in normal conditions, the adrenal androgens have insignificant physiological effects, because of the low amount of secretion both in males and females. In **congenital hyperplasia** of adrenal cortex or tumor of zona

reticularis, an excess quantity of androgens is secreted. In males, it does not produce any special effect because, large quantity of androgens are produced by testes also. But in females, the androgens produce **masculine features**. Some of the androgens are converted into testosterone. Testosterone is responsible for the androgenic activity in adrenogenital syndrome or congenital adrenal hyperplasia.

Q. 7. Write a short note on parathormone.

(TNMGR, Sept. 2007;
Oct. 2011; RGUHS, Oct. 2010)

Ans. Parathormone secreted by parathyroid gland is essential for the maintenance of blood calcium level within a very narrow critical level. Maintenance of blood calcium level is necessary because calcium is an important inorganic ion for many physiological functions.

Source of secretion: Parathormone (PTH) is secreted by the chief cells of the parathyroid glands.

Chemistry: Parathormone is protein in nature, having 84 amino acids. Its molecular weight is 9,500.

Half-life and plasma level: Parathormone has a half-life of 10 minutes. Normal plasma level of PTH is about 1.5 to 5.5 ng/dl.

Synthesis: Parathormone is synthesized from the precursor called **prepro-PTH** containing 115 amino acids. First, the prepro-PTH enters the endoplasmic reticulum of chief cells of parathyroid glands. There it is converted into a prohormone called **pro-PTH**, which contains 96 amino acids. Pro-PTH enters the Golgi apparatus, where it is converted into PTH.

Metabolism: Sixty to seventy percent of PTH is degraded by **Kupffer cells** of liver, by means of proteolysis. Degradation of about 20 to 30% PTH occurs in kidneys and to a lesser extent in other organs.

Actions of parathormone: PTH plays an important role in maintaining blood calcium level. It also controls blood phosphate level.

Actions of parathormone on blood calcium level: Primary action of PTH is to maintain the blood calcium level within the critical range of 9 to 11 mg/dl. The blood calcium level has to be maintained critically because, it is very important for many of the activities in the body. PTH maintains blood calcium level by acting on:

1. Bones
2. Kidney
3. Gastrointestinal tract

Actions of parathormone on blood phosphate level: PTH decreases blood level of phosphate by increasing its urinary excretion. It also acts on bone and GIT.

Regulation of parathormone secretion: Blood level of calcium is the main factor regulating the secretion of PTH. Blood phosphate level also regulates PTH secretion.

Blood level of calcium: Parathormone secretion is inversely proportional to blood calcium level. Increase in blood calcium level decreases PTH secretion. Conditions when PTH secretion decreases are:

1. Excess quantities of calcium in the diet.
 2. Increased vitamin D in the diet.
 3. Increased resorption of calcium from the bones, caused by some other factors such as bone diseases.
- On the other hand, decrease in calcium ion concentration of blood increases PTH secretion, as in the case of rickets, pregnancy and in lactation.

Blood level of phosphate: PTH secretion is directly proportional to blood phosphate level.

Q. 8. Write a short note on ACTH.

Ans. Anterior pituitary controls the activities of adrenal cortex by secreting ACTH. ACTH is mainly concerned with the regulation of cortisol secretion and it plays only a minor role in the regulation of mineralocorticoid secretion. ACTH is secreted by the basophilic chromophilic cells of anterior pituitary. ACTH is a single chained polypeptide with 39 amino acids. The daily output of this hormone is 10 ng and the concentration in plasma is 3 ng/dl. Half-life of ACTH is 10 minutes.

Actions: ACTH is necessary for the structural integrity and secretory activity of adrenal cortex. It has other functions also:

1. Maintenance of structural integrity and vascularization of zona fasciculata and zona reticularis of adrenal cortex.
2. Conversion of cholesterol into pregnenolone, which is the precursor of glucocorticoids. Thus, adrenocorticotrophic hormone is responsible for the synthesis of glucocorticoids.
3. Release of glucocorticoids.
4. Prolongation of glucocorticoid action on various cells.
5. Mobilization of fats from tissues.
6. Melanocyte-stimulating effect.

Mode of action of ACTH: ACTH acts by the formation of cyclic AMP.

Q. 9. Write a note on Cushing syndrome.

(TNMGR, Oct. 2000)

Ans. Cushing syndrome is a disorder characterized by obesity.

Causes: Cushing syndrome is due to the hypersecretion of glucocorticoids, particularly cortisol. It may be either due to pituitary origin or adrenal origin. If it is due to pituitary origin, it is known as **Cushing disease**. If it is due to adrenal origin it is called **Cushing syndrome**.

Pituitary origin: Increased secretion of ACTH causes hyperplasia of adrenal cortex, leading to hypersecretion of glucocorticoid.

Adrenal origin: Cortisol secretion is increased by:

- i. Tumor in zona fasciculata of adrenal cortex.
- ii. Carcinoma of adrenal cortex.
- iii. Prolonged treatment of chronic inflammatory diseases like rheumatoid arthritis, with high dose of exogenous glucocorticoids.
- iv. Prolonged treatment with high dose of ACTH, which stimulates adrenal cortex to secrete excess glucocorticoids.

Signs and Symptoms

- i. **Characteristic feature:** Disproportionate distribution of body fat, resulting in:
 - a. Moon face.
 - b. **Torso:** Fat accumulation in the chest and abdomen. Arms and legs are very slim in proportion to **torso** (torso means trunk of the body).
 - c. Buffalo hump.
 - d. Pot belly.
- ii. **Purple striae:** Due to stretching of abdominal wall by excess subcutaneous fat, rupture of subdermal tissues due to stretching, deficiency of collagen fibers due to protein depletion.
- iii. Thinning of extremities.
- iv. Thinning of skin and subcutaneous tissues.
 - v. **Acanthosis:** Skin disease characterized by darkened skin patches in certain areas such as axilla, neck and groin.
- vi. Pigmentation of skin.
- vii. **Facial plethora:** Facial redness.
- viii. Hirsutism.
- ix. Weakening of muscles because of protein depletion.
 - x. Bone resorption and osteoporosis.
 - xi. Hyperglycemia.
 - xii. Hypertension.
- xiii. Immunosuppression resulting in susceptibility for infection.
- xiv. Poor wound healing.

Tests for Cushing Syndrome

- i. Observation of external features.
- ii. Determination of blood sugar and cortisol levels.
- iii. Analysis of urine for 17-hydroxysteroids.

Treatment for Cushing syndrome

Treatment depends upon the cause of the disease. Treatment may include cortisol-inhibiting drugs, surgical removal of pituitary or adrenal tumor, radiation or chemotherapy.

Q. 10. Write about adrenal medulla.

(TNMGR, March 2002)

Ans. Adrenal medulla is the inner part of adrenal gland and it forms 20% of the mass of adrenal gland. It is made up of interlacing cords of cells known as chromaffin cells. Chromaffin cells are also called pheochrom cells or chromophil cells. Adrenal medulla is formed by two types of chromaffin cells:

1. Adrenaline-secreting cells (90%)
2. Noradrenaline-secreting cells (10%)

Hormones of adrenal medulla: Adrenal medullary hormones are the amines derived from catechol and so these hormones are called catecholamines.

1. Adrenaline or epinephrine
2. Noradrenaline or norepinephrine
3. Dopamine

Catecholamines are synthesized from the amino acid tyrosine in the chromaffin cells of adrenal medulla.

Actions of adrenaline and noradrenaline: Adrenaline and noradrenaline stimulate the nervous system. Adrenaline has significant effects on metabolic functions and both adrenaline and noradrenaline have significant effects on cardiovascular system.

Mode of action of adrenaline and noradrenaline-adrenergic receptors: Actions of adrenaline and noradrenaline are executed by binding with receptors called adrenergic receptors, which are of two types:

1. Alpha-adrenergic receptors, which are subdivided into alpha-1 and alpha-2 receptors.
2. Beta-adrenergic receptors, which are subdivided into beta-1 and beta-2 receptors.

Actions: Circulating adrenaline and noradrenaline have similar effect of sympathetic stimulation. But, the effect of adrenal hormones is prolonged 10 times more than that of sympathetic stimulation.

1. **On metabolism (via alpha and beta receptors):** Adrenaline influences the metabolic functions more than noradrenaline.

- i. *General metabolism*: It increases basal metabolic rate. So, it is said to be a calorogenic hormone.
- ii. *Carbohydrate metabolism*: Adrenaline increases the blood glucose level by increasing the glycogenolysis in liver and muscle.
- iii. *Fat metabolism*: Adrenaline causes mobilization of free fatty acids from adipose tissues.
2. **On blood (via beta receptors)**: Adrenaline decreases blood coagulation time. It increases RBC count in blood.
3. **On heart (via beta receptors)**: It increases overall activity of the heart, i.e.
 - i. Heart rate (chronotropic effect).
 - ii. Force of contraction (inotropic effect).
 - iii. Excitability of heart muscle (bathmotropic effect).
 - iv. Conductivity in heart muscle (dromotropic effect).
4. **On blood vessels (via alpha and beta-2 receptors)**: Noradrenaline has strong effects on blood vessels. It causes constriction of blood vessels throughout the body via alpha receptors. So it is called 'general vasoconstrictor'. Adrenaline also causes constriction of blood vessels. However, it causes dilatation of blood vessels in skeletal muscle, liver and heart through beta-2 receptors. So, the total peripheral resistance is decreased by adrenaline.
5. **On blood pressure (via alpha and beta receptors)**: Adrenaline increases systolic blood pressure, but it decreases diastolic blood pressure. Noradrenaline increases diastolic pressure.
6. **On respiration (via beta-2 receptors)**: Adrenaline increases rate and force of respiration.
7. **On skin (via alpha and Beta-2 receptors)**: Adrenaline causes contraction of arrector pili. It also increases the secretion of sweat.
8. **On skeletal muscle (via alpha and beta-2 receptors)**: Adrenaline causes severe contraction and quick fatigue of skeletal muscle. It increases glycogenolysis and release of glucose from muscle into blood.
9. **On smooth muscle (via alpha and beta receptors)**: Catecholamines cause contraction of smooth muscles in the following organs:
 - i. Splenic capsule
 - ii. Sphincters of gastrointestinal tract (GIT)
 - iii. Arrector pili of skin
 - iv. Gallbladder
 - v. Uterus
 - vi. Dilator pupillae of iris

Catecholamines cause relaxation of smooth muscles in the following organs

- i. Non-sphincteric part of GIT (esophagus, stomach and intestine)

- ii. Bronchioles
- iii. Urinary bladder

10. **On central nervous system (via beta receptors)**: Adrenaline increases the activity of brain. Adrenaline secretion increases during 'fight or flight reactions' after exposure to stress.
11. **Other effects of catecholamines**
 - i. *On salivary glands (via alpha and beta-2 receptors)*: Cause vasoconstriction in salivary gland, leading to mild increase in salivary secretion.
 - ii. *On sweat glands (via beta-2 receptors)*: Increase the secretion of apocrine sweat glands.
 - iii. *On lacrimal glands (via alpha receptors)*: Increase the secretion of tears.
 - iv. *On ACTH secretion (via alpha receptors)*: Adrenaline increases ACTH secretion.
 - v. *On nerve fibers (via alpha receptors)*: Electrical activity is accelerated.
 - vi. *On renin secretion (via beta receptors)*: Increase the rennin secretion from juxtaglomerular apparatus of the kidney.

Regulation of secretion of adrenaline and noradrenaline:

Adrenaline and noradrenaline are secreted from adrenal medulla in small quantities even during rest. During stress conditions, due to sympathoadrenal discharge, a large quantity of catecholamines is secreted. These hormones prepare the body for fight or flight reactions. Catecholamine secretion increases during exposure to cold and hypoglycemia also.

Dopamine: Dopamine is secreted by adrenal medulla. Dopamine is also secreted by dopaminergic neurons in some areas of brain, particularly basal ganglia. In brain, this hormone acts as a neurotransmitter. Injected dopamine produces the following effects:

1. Vasoconstriction by releasing norepinephrine.
2. Vasodilatation in mesentery.
3. Increase in heart rate via beta receptors.
4. Increase in systolic blood pressure. Dopamine does not affect diastolic blood pressure.

Deficiency of dopamine in basal ganglia produces nervous disorder called parkinsonism.

Applied Physiology

Pheochromocytoma: Pheochromocytoma is a condition characterized by hypersecretion of catecholamines. Pheochromocytoma is caused by tumor of chromophil cells in adrenal medulla.

Signs and symptoms: Characteristic feature of pheochromocytoma is hypertension. Other features: Anxiety, chest pain, fever, headache, hyperglycemia,

metabolic disorders, nausea, vomiting, palpitation, polyuria, glucosuria, sweating, flushing, tachycardia, and weight loss.

Q. 11. Write a short note on neurohormones.

(TNMGR, Sept. 2002; March 2008)

Ans. It is a chemical substance that is released by the nerve cell directly into the blood and transported to a distant target cells. For example, oxytocin, antidiuretic hormone and releasing hormones secreted by the hypothalamus. Some of the chemical mediators act as more than one type of chemical messengers. For example, noradrenaline and dopamine function as classical hormones as well as neurotransmitters. Similarly, histamine acts as neurotransmitter and paracrine messenger.

Q. 12. Write a note on physiology of regulation of blood glucose level.

(TNMGR, April 1997; Sept. 2007; April 2012)

Ans. Normal blood glucose level: In the early morning after overnight fasting, the blood glucose level is low ranging between 70 and 110 mg/dl of blood. Between first and second hour after meals (postprandial), the blood glucose level rises to 100 to 140 mg/dl. Insulin is the only hormone that reduces the blood glucose level and it is called the **antidiabetogenic hormone**.

1. **Role of liver in the maintenance of blood glucose level:** When blood glucose level increases after a meal, the excess glucose is converted into glycogen and stored in liver. Afterwards, when blood glucose level falls, the glycogen in liver is converted into glucose and released into the blood.
2. **Role of insulin in the maintenance of blood glucose level:** Insulin decreases the blood glucose level and it is the only antidiabetic hormone available in the body.
3. **Role of glucagon in the maintenance of blood glucose level:** Glucagon increases the blood glucose level.
4. **Role of other hormones in the maintenance of blood glucose level:** Other hormones which increase the blood glucose level are:
 - a. Growth hormone
 - b. Thyroxine
 - c. Cortisol
 - d. Adrenaline

Q. 13. Write about functions of insulin.

(TNMGR, April 1998; March 2007; Sept. 2008; April 2012)

Ans. Insulin is the important hormone that is concerned with the regulation of carbohydrate metabolism and blood glucose level. It is also concerned with the metabolism of proteins and fats.

1. **On carbohydrate metabolism:** Insulin decreases the blood glucose level by:
 - i. Facilitating transport and uptake of glucose by the cells.
 - ii. Increasing the peripheral utilization of glucose.
 - iii. Increasing the storage of glucose by converting it into glycogen in liver and muscle.
 - iv. Inhibiting glycogenolysis.
 - v. Inhibiting gluconeogenesis.
2. **On protein metabolism:** Insulin facilitates the synthesis and storage of proteins and inhibits the cellular utilization of proteins.
3. **On fat metabolism**
 - i. Synthesis of fatty acids and triglycerides.
 - ii. Transport of fatty acids into adipose tissue.
 - iii. Insulin promotes the storage of fat in adipose tissue by inhibiting the enzymes which degrade the triglycerides.
4. **On growth:** Along with growth hormone, insulin promotes growth of body by its anabolic action on proteins. It enhances the transport of amino acids into the cell and synthesis of proteins in the cells. It also has the protein-sparing effect.

6. GASTROINTESTINAL SYSTEM

Q. 1. Write briefly on the composition and functions of saliva and the physiology of its secretion.

(TNMGR, April 1995; Oct. 2012; Pacific Uni., May 2010; RGUHS, May 2012)

Q. Write about physiology and mechanism of secretion of saliva.

(TNMGR, March 2009; BFUHS, May 2009, 2010; RUHS, May 2015)

Q. Describe the composition, properties and functions of saliva. Discuss its role in the oral defense mechanism.

(TNMGR, Sept. 2007; BFUHS, Nov. 2008, 2012; RGUHS, Oct. 2010; MUHS, Nov. 2015; HP, May 2015)

Q. Discuss the role of saliva in oral health.

(TNMGR, March 2010; April 2012; RGUHS, Oct. 2010; MAHE, Nov. 1999)

Ans. Composition of saliva

- a. Water—99.5%
- b. Solids—0.5%

1. Organic substances

- a. **Enzymes:** Amylase, maltase, lingual lipase, lysozyme, phosphatase, carbonic anhydrase, and kallikrein.

- b. *Others*: Mucin, albumin, proline-rich proteins, lactoferrin, IgA, blood group antigens, free amino acids, and non-protein nitrogenous substance.
- 2. **Inorganic substances**: Na, Ca, K, bicarbonates, Br, Cl, F, and PO_4 .
- 3. **Gases**: O_2 , CO_2 , and N.

Properties of Saliva

1. **Volume**: 1000–1500 ml of saliva is secreted per day and it is approximately about 1 ml/minute. Contribution by each major salivary gland is:
 - i. *Parotid glands*: 25%
 - ii. *Submandibular glands*: 70%
 - iii. *Sublingual glands*: 5%
2. **Reaction**: Mixed saliva from all the glands is slightly acidic with pH of 6.35 to 6.85.
3. **Specific gravity**: It ranges between 1.002 and 1.012.
4. **Tonicity**: Saliva is hypotonic to plasma.

Functions of Saliva

1. **Preparation of food for swallowing**: When food is taken into the mouth; it is moistened and dissolved by saliva. It facilitates chewing. Mucin of saliva lubricates the bolus and facilitates swallowing.
2. **Appreciation of taste**: By its solvent action, saliva dissolves the solid food substances, so that the dissolved substances can stimulate the taste buds.
3. **Digestive function**: Saliva has three digestive enzymes, namely salivary amylase, maltase and lingual lipase.

Salivary amylase: Salivary amylase is a carbohydrate digesting (amylolytic) enzyme. It acts on cooked or boiled starch and converts it into **dextrin** and **maltose**. Optimum pH necessary for the activation of salivary amylase is 6. Salivary amylase cannot act on **cellulose**.

Maltase: Maltase is present only in traces in human saliva and it converts maltose into glucose.

Lingual lipase: Lingual lipase is a lipid-digesting (lipolytic) enzyme. It is secreted from serous glands situated on the posterior aspect of tongue. It digests milk fats (**pre-emulsified fats**). It hydrolyzes triglycerides into fatty acids and diacylglycerol.

4. **Cleansing and protective functions**
 - i. Due to the constant secretion of saliva, the mouth and teeth are rinsed and kept free off food debris, shed epithelial cells and foreign particles.
 - ii. Enzyme lysozyme of saliva kills some bacteria such as *Staphylococcus*, *Streptococcus* and *Brucella*.
 - iii. **Proline-rich proteins** neutralize the toxic substances such as tannins.

- iv. Lactoferrin of saliva also has antimicrobial property.
- v. Proline-rich proteins and lactoferrin protect the teeth by stimulating enamel formation.
- vi. Immunoglobulin IgA in saliva also has antibacterial and antiviral actions.
- vii. Mucin present in the saliva protects the mouth by lubricating the mucous membrane of mouth.
5. **Role in speech**: By moistening and lubricating soft parts of mouth and lips, saliva helps in speech.
6. **Excretory function**: Many substances, both organic and inorganic, are excreted in saliva.
7. **Regulation of body temperature**: In dogs and cattle, excessive dripping of saliva helps in the loss of heat and regulation of body temperature.
8. **Regulation of water balance**: When the body water content decreases, salivary secretion also decreases. This causes dryness of the mouth and induces thirst.

Regulation of salivary secretion: Salivary gland is supplied by both parasympathetic and sympathetic divisions of autonomic nervous system.

A. Parasympathetic Fibers

1. **Parasympathetic fibers to submandibular and sublingual glands**: Parasympathetic preganglionic fibers to submandibular and sublingual glands arise from the superior salivatory nucleus, situated in pons. The preganglionic fibers run through nervus intermedius of Wrisberg, geniculate ganglion, the motor fibers of facial nerve, chorda tympani branch of facial nerve and lingual branch of trigeminal nerve and finally reach the submandibular ganglion. Postganglionic fibers arising from this ganglion supply the submandibular and sublingual glands.
2. **Parasympathetic fibers to parotid gland**: Parasympathetic preganglionic fibers to parotid gland arise from inferior salivatory nucleus situated in the upper part of medulla oblongata. The fibers pass through the tympanic branch of glossopharyngeal nerve, tympanic plexus and lesser petrosal nerve and end in otic ganglion. Postganglionic fibers arise from this ganglion and supply the parotid gland by passing through auriculotemporal branch in mandibular division of trigeminal nerve.

Function of parasympathetic fibers: Stimulation of parasympathetic fibers of salivary glands causes secretion of saliva with large quantity of water.

B. Sympathetic Fibers

Sympathetic preganglionic fibers to salivary glands arise from the lateral horns of first and second thoracic

segments of spinal cord. The fibers leave the cord through the anterior nerve roots and end in superior cervical ganglion of the sympathetic chain. Post-ganglionic fibers arise from this ganglion and are distributed to the salivary glands along the nerve plexus, around the arteries supplying the glands.

Function of sympathetic fibers: Stimulation of sympathetic fibers causes secretion of saliva, which is thick and rich in organic constituents such as mucus.

Reflex Regulation of Salivary Secretion

1. **Unconditioned reflex:** It does not need any previous experience.
2. **Conditioned reflex:** Conditioned reflex is the one that is acquired by experience and it needs previous experience. The stimuli for this reflex are the sight, smell, hearing or thought of food.

Q. 2. Write a short note on mastication.

(TNMGR, Nov. 2001; BFUHS, Oct. 2010)

Ans. Mastication or **chewing** is the first mechanical process in the gastrointestinal tract (GIT), by which the food substances are torn or cut into small particles and crushed or ground into a soft **bolus**.

Significances of Mastication

1. Breakdown of foodstuffs into smaller particles.
2. Mixing of saliva with food substances thoroughly.
3. Lubrication and moistening of dry food by saliva, so that the bolus can be easily swallowed
4. Appreciation of taste of the food.

Muscles and Movements of Mastication

Muscles of Mastication

1. Masseter muscle
2. Temporal muscle
3. Pterygoid muscles
4. Buccinator muscle

Movements of Mastication

1. Opening and closure of mouth
2. Rotational movements of jaw
3. Protraction and retraction of jaw

Control of Mastication

Action of mastication is mostly a reflex process. It is carried out voluntarily also. The center for mastication is situated in medulla and cerebral cortex. Muscles of mastication are supplied by mandibular division of 5th cranial (trigeminal) nerve.

Q. 3. Write a note on deglutition.

(TNMGR, Oct. 1999; March 2002; April 2012; Oct. 2013; BFUHS, May 2009; Oct. 2010; RGUHS, May 2011; UHSR, April 2013)

Ans. Deglutition or swallowing is the process by which food moves from mouth into stomach.

Stages of Deglutition

- a. **Oral stage or first stage:** Oral stage of deglutition is a voluntary stage. In this stage, the bolus from mouth passes into pharynx by means of series of actions.
 1. Bolus is placed over posterodorsal surface of the tongue. It is called the preparatory position.
 2. Anterior part of tongue is retracted and depressed.
 3. Posterior part of tongue is elevated and retracted against the hard palate. This pushes the bolus backwards into the pharynx.
 4. Forceful contraction of tongue against the palate produces a positive pressure in the posterior part of oral cavity. This also pushes the food into pharynx.
- b. **Pharyngeal stage or second stage:** Pharyngeal stage is an involuntary stage. In this stage, the bolus is pushed from pharynx into the esophagus. Bolus from the pharynx can enter into four paths:
 1. Back into mouth
 2. Upward into nasopharynx
 3. Forward into larynx
 4. Downward into esophagus

However, due to various coordinated movements, bolus is made to enter only the esophagus.

- c. **Esophageal stage or third stage:** Esophageal stage is also an involuntary stage. In this stage, food from esophagus enters the stomach. Esophagus forms the passage for movement of bolus from pharynx to the stomach. Movements of esophagus are specifically organized for this function and the movements are called peristaltic waves. When bolus reaches the esophagus, the peristaltic waves are initiated. Usually, two types of peristaltic contractions are produced in esophagus—(i) primary peristaltic contractions, (ii) secondary peristaltic contractions.

Q. 4. Write a short note on deglutition reflex.

(TNMGR, Sept. 2009; April 2013)

Ans. Though the beginning of swallowing is a voluntary act, later it becomes involuntary and is carried out by a reflex action called deglutition reflex. It occurs during the pharyngeal and esophageal stages.

Stimulus: When the bolus enters the oropharyngeal region, the receptors present in this region are stimulated.

Afferent fibers: Afferent impulses from the oropharyngeal receptors pass via the glossopharyngeal nerve fibers to the deglutition center.

Center: Deglutition center is at the floor of the fourth ventricle in medulla oblongata of brain.

Efferent fibers: Impulses from deglutition center travel through glossopharyngeal and vagus nerves (parasympathetic motor fibers) and reach soft palate, pharynx and esophagus. The glossopharyngeal nerve is concerned with pharyngeal stage of swallowing. The vagus nerve is concerned with esophageal stage.

Response: The reflex causes upward movement of soft palate, to close nasopharynx and upward movement of larynx, to close respiratory passage so that bolus enters the esophagus. Now the peristalsis occurs in esophagus, pushing the bolus into stomach.

Q. 5. Write a short note on digestive enzymes.

(TNMGR, March 2007)

Ans.

A. Digestive Enzymes of Saliva

Saliva has three digestive enzymes, namely salivary amylase, maltase and lingual lipase:

1. **Salivary amylase:** Salivary amylase is a carbohydrate-digesting (amylolytic) enzyme. It acts on cooked or boiled starch and converts it into dextrin and maltose. Salivary amylase cannot act on cellulose.
2. **Maltase:** Maltase is present only in traces in human saliva and it converts maltose into glucose.
3. **Lingual lipase:** Lingual lipase is a lipid-digesting (lipolytic) enzyme. It is secreted from serous glands situated on the posterior aspect of tongue. It digests milk fats (pre-emulsified fats). It hydrolyzes triglycerides into fatty acids and diacylglycerol.

B. Digestive Enzymes of Gastric Juice

1. **Pepsin:** Pepsin converts proteins into proteoses, peptones and polypeptides. Pepsin also causes curdling and digestion of milk (casein).
2. **Gastric lipase:** Gastric lipase is a tributyrase and it hydrolyzes tributyrin (butter fat) into fatty acids and glycerols.
3. **Gelatinase:** Degrades type I and type V gelatin and type IV and V collagen into peptides.
4. **Urase:** Acts on urea and produces ammonia.
5. **Gastric amylase:** Degrades starch.
6. **Renin:** Curdles milk (present in animals only).

C. Digestive Enzymes of Pancreatic Juice

1. **Trypsin:** It acts on proteins and the end products are proteoses and polypeptides.

2. **Chymotrypsin:** It acts on proteins and the end products are polypeptides.
3. **Carboxypeptidases:** It acts on polypeptides and the end products are amino acids.
4. **Nucleases:** It acts on RNA and DNA and the end products are mononucleotides.
5. **Elastase:** It acts on elastin and the end products are amino acids.
6. **Collagenase:** It acts on collagen and the end products are amino acids.
7. **Pancreatic lipase:** It acts on triglycerides and the end products are monoglycerides and fatty acids.
8. **Cholesterol ester hydrolase:** It acts on cholesterol ester and the end products are cholesterol and fatty acids.
9. **Phospholipase A:** It acts on phospholipids and the end products are lysophospholipids.
10. **Phospholipase B:** It acts on lysophospholipids and the end products are phosphoryl choline and free fatty acids.
11. **Pancreatic lipase:** It acts on starch and the end products are dextrin and maltose.

D. Digestive Enzymes of Succus Entericus

1. **Peptidases:** It acts on peptides and the end products are amino acids.
2. **Sucrase:** It acts on sucrose and the end products are amino acids.
3. **Maltase:** It acts on maltose and maltotriose and the end products are glucose.
4. **Lactase:** It acts on lactose and the end products are galactose and glucose.
5. **Dextrinase:** It acts on dextrin, maltose, maltriose and the end products are glucose.
6. **Trehalase:** It acts on trehalose and the end products are glucose.
7. **Intestinal lipase:** It acts on triglycerides and the end products are fatty acids.

Q. 6. Write about functions of liver.

(TNMGR, March 2009; RGUHS, May 2011)

Ans. Liver is the largest gland and one of the vital organs of the body:

1. **Metabolic function:** Liver is the organ where metabolism of carbohydrates, proteins, fats, vitamins and many hormones are carried out.
2. **Storage function:** Many substances like glycogen, amino acids, iron, folic acid and vitamins A, B₁₂ and D are stored in liver.
3. **Synthetic function:** Liver produces glucose by gluconeogenesis. It synthesizes all the plasma

proteins and other proteins (except immunoglobulins) such as clotting factors, complement factors and hormone binding proteins. It also synthesizes steroids, somatomedin and heparin.

4. **Secretion of bile:** Liver secretes bile which contains bile salts, bile pigments, cholesterol, fatty acids and lecithin. Bile salts are required for digestion and absorption of fats in the intestine.
5. **Excretory function:** Liver excretes cholesterol, bile pigments, heavy metals, toxins, bacteria and virus through bile.
6. **Heat production:** Liver is the organ where maximum heat is produced.
7. **Hemopoietic function:** In fetus, liver produces the blood cells. It produces thrombopoietin that promotes production of thrombocytes.
8. **Hemolytic function:** The senile RBCs are destroyed by Kupffer cells of liver.
9. **Inactivation of hormones and drugs:** Liver catabolizes the hormones and inactivates the drugs.
10. **Defensive and detoxification functions:** Reticulo-endothelial cells (Kupffer cells) of the liver play an important role in the defense of the body.
 - i. Foreign bodies are swallowed and digested by reticuloendothelial cells of liver by means of phagocytosis.
 - ii. Also produce substances like interleukins and tumor necrosis factors, which activate the immune system of the body.
 - iii. Liver cells are involved in the removal of toxic property of various harmful substances.

Q. 7. Write about digestion of proteins.

(TNMGR, Nov. 2001)

Ans. Foodstuffs containing high protein content are meat, fish, egg and milk. Proteins are also available in wheat, soybeans, oats and various types of pulses. Proteins present in common foodstuffs are:

1. **Wheat:** Glutenin and gliadin, which constitute gluten.
2. **Milk:** Casein, lactalbumin, albumin and myosin.
3. **Egg:** Albumin and vitellin.
4. **Meat:** Collagen, albumin and myosin.

Dietary proteins are formed by long chains of amino acids, bound together by peptide linkages.

Digestion of proteins: Enzymes responsible for the digestion of proteins are called **proteolytic enzymes**.

In the mouth: Digestion of proteins does not occur in mouth, since saliva does not contain any proteolytic enzymes.

In the stomach: **Pepsin** is the only proteolytic enzyme in gastric juice. **Renin** is also present in gastric juice. But it is absent in human.

In the small intestine: Most of the proteins are digested in the duodenum and jejunum by the proteolytic enzymes of the pancreatic juice and succus entericus.

Proteolytic enzymes in pancreatic juice: Pancreatic juice contains **trypsin**, **chymotrypsin** and **carboxypeptidases**. Trypsin and chymotrypsin are called **endopeptidases**, as these two enzymes break the interior bonds of the protein molecules—**dipeptidases**, **tripeptidases** and **aminopeptidases**.

Final products of protein digestion: Final products of protein digestion are the amino acids, which are absorbed into blood from intestine.

Q. 8. Write about digestion of carbohydrates.

(TNMGR, April 2003)

Ans. Human diet contains three types of carbohydrates:

1. **Polysaccharides:** Large polysaccharides are glycogen, amylose and amylopectin, which are in the form of starch (glucose polymers). Glycogen is available in **non-vegetarian diet**. Amylose and amylopectin are available in **vegetarian diet**.
2. **Disaccharides:** Two types of disaccharides are available in the diet.
 - i. Sucrose (glucose + fructose)
 - ii. Lactose (glucose + galactose)
3. **Monosaccharides:** Monosaccharides consumed in human diet are mostly glucose and fructose. Other carbohydrates in the diet include:
 - i. Alcohol
 - ii. Lactic acid
 - iii. Pyruvic acid
 - iv. Pectins
 - v. Dextrins
 - vi. Carbohydrates in meat

Diet also contains large amount of **cellulose**, which cannot be digested in the human.

Digestion of Carbohydrates

In the mouth: Enzymes involved in the digestion of carbohydrates are known as **amylolytic enzymes**. The only amylolytic enzyme present in saliva is the salivary amylase or ptyalin.

In the stomach: Gastric juice contains a **weak amylase**, which plays a minor role in digestion of carbohydrates.

In the intestine: Amylolytic enzymes are derived from pancreatic juice and succus entericus.

Amylolytic enzyme in pancreatic juice: Pancreatic amylase.

Amylolytic enzymes in succus entericus: Maltase, sucrase, lactase, dextrinase and trehalase.

Final products of carbohydrate digestion: Final products of carbohydrate digestion are mono-saccharides, which are glucose, fructose and galactose.

Q. 9. Write in detail about the calcium and phosphate mechanism.

(BFUHS, May 2011; Nov. 2011; RGUHS, Nov. 2011; May 2013; RUHS, May 2015; MUHS, June 2015)

Q. Describe calcium homeostasis and its influence on oral tissues.

(TNMGR, Sept. 2007; March 2008; Oct. 2012; BFUHS, May 2010; HP, May 2013)

Q. Describe the role of hormones in regulations of blood calcium levels. (Nagpur Uni. 1991)

Ans. Calcium is very essential for many activities in the body such as:

1. Bone and teeth formation
2. Neuronal activity
3. Skeletal muscle activity
4. Cardiac activity
5. Smooth muscle activity
6. Secretory activity of the glands
7. Cell division and growth
8. Coagulation of blood

Normal value: Normal blood calcium level ranges between 9 and 11 mg/dl.

Types of calcium: Calcium in plasma is present in three forms in plasma:

- i. **Ionized or diffusible calcium:** Found freely in plasma and forms about 50% of plasma calcium. It is essential for vital functions such as neuronal activity, muscle contraction, cardiac activity, secretions in the glands, blood coagulation, etc.
- ii. **Non-ionized or non-diffusible calcium:** It is about 8 to 10% of plasma calcium
- iii. **Calcium bound to albumin:** Forms about 40 to 42% of plasma calcium.

Calcium in bones: Calcium is constantly removed from bone and deposited in bone. Bone calcium is present in two forms:

- i. **Rapidly exchangeable calcium or exchangeable calcium:** Available in small quantity in bone and helps to maintain the plasma calcium level.

- ii. **Slowly exchangeable calcium or stable calcium:** Available in large quantity in bones and helps in bone remodeling.

Source of Calcium

1. **Dietary source:** Percentage of calcium in different food substance is:

Whole milk = 10%

Low fat milk = 18%

Cheese = 27%

Other dairy products = 17%

Vegetables = 7%

Other substances such as meat, egg, grains, sugar, coffee, tea, chocolate, etc. = 21%

2. **From bones:** Besides dietary calcium, blood also gets calcium from bone by resorption.

Daily requirements of calcium

1 to 3 years = 500 mg

4 to 8 years = 800 mg

9 to 18 years = 1,300 mg

19 to 50 years = 1,000 mg

51 years and above = 1,200 mg

Pregnant ladies and lactating mother = 1,300 mg

Absorption and excretion of calcium: Calcium taken through dietary sources is absorbed from gastrointestinal tract (GIT) into blood and distributed to various parts of the body. Depending upon the blood level, the calcium is either deposited in the bone or removed from the bone. Calcium is excreted from the body through urine and feces.

Absorption from gastrointestinal tract: Calcium is absorbed from duodenum by carrier mediated active transport and from the rest of the small intestine, by facilitated diffusion. Vitamin D is essential for the absorption of calcium from GIT.

Excretion: While passing through the kidney, large quantity of calcium is filtered in the glomerulus. From the filtrate, 98–99% of calcium is reabsorbed from renal tubules into the blood. Only a small quantity is excreted through urine. Most of the filtered calcium is reabsorbed in the distal convoluted tubules and proximal part of collecting duct.

In distal convoluted tubule, parathormone increases the reabsorption. In collecting duct, vitamin D increases the reabsorption and calcitonin decreases reabsorption. About 1,000 mg of calcium is excreted daily. Out of this, 900 mg is excreted through feces and 100 mg through urine.

Regulation of Blood Calcium Level

1. **Parathormone:** Its main function is to increase the blood calcium level by mobilizing calcium from bone.
2. **1, 25-dihydroxycholecalciferol (calcitriol):** Its main action is to increase the blood calcium level by increasing the calcium absorption from the small intestine.
3. **Calcitonin:** It reduces the blood calcium level mainly by decreasing bone resorption.
4. **Growth hormone:** Growth hormone increases the blood calcium level by increasing the intestinal calcium absorption.
5. **Glucocorticoids:** Glucocorticoids (cortisol) decrease blood calcium by inhibiting intestinal absorption and increasing the renal excretion of calcium.

Phosphate Metabolism

Phosphorus (P) is an essential mineral that is required by every cell in the body for normal function. Phosphorus is present in many food substances, such as peas, dried beans, nuts, milk, cheese and butter. Inorganic phosphorus (Pi) is in the form of the **phosphate** (PO_4). The majority of the phosphorus in the body is found as phosphate. Phosphorus is also the body's source of phosphate. In body, phosphate is the most abundant intracellular anion.

Importance of Phosphate

1. Phosphate is an important component of many organic substances such as ATP, DNA, RNA and many intermediates of metabolic pathways.
2. Along with calcium, it forms an important constituent of bone and teeth.
3. It forms a buffer in the maintenance of acid–base balance.

Normal value: Normal plasma level of phosphate is 4 mg/dl.

Regulation of phosphate level: Blood phosphate level is regulated by:

1. **Parathormone:** Parathormone stimulates resorption of phosphate from bone and increases its urinary excretion. It also increases the absorption of phosphate from gastrointestinal tract through calcitriol. The overall action of parathormone decreases the plasma level of phosphate.
2. **Calcitonin:** Calcitonin also decreases the plasma level of phosphate by inhibiting bone resorption and stimulating the urinary excretion.

3. **1, 25-dihydroxycholecalciferol:** Calcitriol hormone increases absorption of phosphate from small intestine.
4. **Growth hormone:** Growth hormone increases the blood phosphate level by increasing the intestinal phosphate absorption.
5. **Glucocorticoids:** Glucocorticoids (cortisol) decreases blood phosphate by inhibiting intestinal absorption and increasing the renal excretion of phosphate.

Q. 10. Write a note on bone remodeling.

(RGUHS, Nov. 2011)

Q. Write a short note on bone metabolism.

(HP, May 2010)

Ans. Bone remodeling is a dynamic lifelong process in which old bone is resorbed and new bone is formed. Usually, it takes place in groups of bone cells called the **basic multicellular units (BMU)**.

Processes of Bone Remodeling

Bone resorption-osteoclastic activity: Osteoclastic activity is the process that involves destruction of bone matrix, followed by removal of calcium. Osteoclasts are responsible for bone resorption by their osteoclastic activity. Part of the bone to be resorbed is known as bone resorbing compartment. The osteoclast present in this compartment attaches itself to the periosteal or endosteal surface of bone through villi-like membranous extensions. This process is mediated by the surface receptors called **integrins**. At the point of attachment, a ruffled border is formed by folding of the cell membrane. Resorption of that particular compartment occurs by some substances released from membranous extensions of osteoclasts such as:

1. Collagenase
2. Phosphatase
3. Lysosomal enzymes
4. Acids like citric acid and lactic acid

Bone formation-osteoblastic activity: Osteoblastic activity is the process which involves the synthesis of collagen and formation of bone matrix that is mineralized. Osteoblasts synthesize and release collagen into the shallow cavity formed after resorption in the bone resorbing compartment. The collagen fibers arrange themselves in regular units and form the organic matrix called osteoid.

Mineralization: Mineralization starts about 10–12 days after the formation of osteoid. First, a large quantity of calcium phosphate is deposited. Afterwards, the hydroxide and bicarbonate ions are gradually added

causing the formation of **hydroxyapatite crystals**. The process of mineralization is accelerated by the enzyme alkaline phosphatase, secreted by osteoblast. The process also requires the availability of adequate amount of calcium and phosphate in the ECF.

The completely mineralized bone surrounds the osteoblast. Now, the synthetic activity of osteoblast is reduced slowly and the cell is converted into osteocytes. Later, the bone is arranged in concentric lamellae on the inner surface of the cavity. At the end of the formation of new bone, the cavity is reduced to form haversian canal.

Significance of Bone Remodeling

In children

1. Thickness of bone increases.
2. Bone obtains strength in proportion to the growth.
3. Shape of the bone is realtered in relation to growth of the body.

In adults

1. Toughness of bone is maintained.
2. Mechanical integrity of skeleton is ensured throughout life.
3. Blood calcium level is maintained.

Regulation of bone remodeling: Bone remodeling occurs continuously throughout life. So, a balance is maintained always between the bone resorption and bone formation. However, in persons like athletes, soldiers and others, in whom the bone stress is more, the bone becomes heavy and strong. It is because of the stimulation of osteoblastic activity and mineralization of bone by repeated physical stress. Apart from the physical stress, a variety of hormonal substances and growth factors are involved in regulation of bone resorption and bone formation.

7. RENAL SYSTEM

Q. 1. Write a note on juxtaglomerular apparatus.

(TNMGR, April 2001)

Ans. Juxtaglomerular apparatus is a specialized organ situated near the glomerulus of each nephron (juxta = near).

Structure of juxtaglomerular apparatus: Juxtaglomerular apparatus is formed by three different structures:

1. Macula densa
2. Extraglomerular mesangial cells
3. Juxtaglomerular cells

Macula densa: Macula densa is the end portion of thick ascending segment before it opens into distal

convoluted tubule. It is situated between afferent and efferent arterioles of the same nephron. It is very close to afferent arteriole. Macula densa is formed by tightly packed cuboidal epithelial cells.

Extraglomerular mesangial cells: Extraglomerular mesangial cells are situated in the triangular region bound by afferent arteriole, efferent arteriole and macula densa. These cells are also called **agranular cells**, **lakis cells** or **Goormaghtigh cells**.

Glomerular mesangial cells: Besides extraglomerular mesangial cells there is another type of mesangial cells situated in between glomerular capillaries called **glomerular mesangial** or **intraglomerular mesangial cells**. Glomerular mesangial cells support the glomerular capillary loops by surrounding the capillaries in the form of a cellular network.

These cells play an important role in regulating the glomerular filtration by their contractile property. Glomerular mesangial cells are phagocytic in nature. These cells also secrete glomerular **interstitial matrix**, prostaglandins and cytokines.

Juxtaglomerular cells: Juxtaglomerular cells are specialized smooth muscle cells situated in the wall of afferent arteriole just before it enters the Bowman capsule. These smooth muscle cells are mostly present in tunica media and tunica adventitia of the wall of the afferent arteriole. Juxtaglomerular cells are also called **granular cells**.

Polar cushion or polkissen: Juxtaglomerular cells form a thick cuff called **polar cushion** or **polkissen** around the afferent arteriole before it enters the Bowman capsule.

Functions of juxtaglomerular apparatus: Primary function of juxtaglomerular apparatus is the secretion of hormones. It also regulates the glomerular blood flow and glomerular filtration rate.

Secretion of hormones: Juxtaglomerular apparatus secretes two hormones:

1. Renin
2. Prostaglandin

Secretion of other Substances

1. Extraglomerular mesangial cells of juxtaglomerular apparatus secrete cytokines like interleukin-2 and tumor necrosis factor.
2. Macula densa secretes thromboxane A_2 .

Regulation of glomerular blood flow and glomerular filtration rate: Macula densa of juxtaglomerular

apparatus plays an important role in the feedback mechanism called **tubuloglomerular feedback** mechanism, which regulates the renal blood flow and glomerular filtration rate.

Q. 2. Write a short note on glomerular filtration.

(TNMGR, April 2003)

Ans. Glomerular filtration is the process by which the blood is filtered while passing through the glomerular capillaries by filtration membrane.

Filtration membrane: Filtration membrane is formed by three layers:

1. **Glomerular capillary membrane:** Glomerular capillary membrane is formed by single layer of endothelial cells, which are attached to the basement membrane. The capillary membrane has many pores called fenestrae or filtration pores.
2. **Basement membrane:** Basement membrane of glomerular capillaries and the basement membrane of visceral layer of Bowman capsule fuse together. The fused basement membrane separates the endothelium of glomerular capillary and the epithelium of visceral layer of Bowman capsule.
3. **Visceral layer of Bowman capsule:** This layer is formed by a single layer of flattened epithelial cells resting on a basement membrane. Each cell is connected with the basement membrane by cytoplasmic extensions called **pedicles** or **feet**. Epithelial cells with pedicles are called **podocytes**. Pedicles interdigitate leaving small cleft-like spaces in between. The cleft-like space is called **slit pore** or **filtration slit**. Filtration takes place through these slit pores.

Process of glomerular filtration: When blood passes through glomerular capillaries, the plasma is filtered into the Bowman capsule. All the substances of plasma are filtered except the plasma proteins. The filtered fluid is called **glomerular filtrate**.

Ultrafiltration: Glomerular filtration is called ultrafiltration because even the minute particles are filtered.

Glomerular filtration rate: Glomerular filtration rate (GFR) is defined as the total quantity of filtrate formed in all the nephrons of both the kidneys in the given unit of time. Normal GFR is 125 ml/minute or about 180 L/day.

Filtration fraction: Filtration fraction is the fraction of the renal plasma, which becomes the filtrate. It is the ratio between renal plasma flow and glomerular filtration rate. It is expressed in percentage. Normal filtration fraction varies from 15–20%.

Pressures determining filtration

1. **Glomerular capillary pressure:** Glomerular capillary pressure is the pressure exerted by the blood in glomerular capillaries. It is about 60 mm Hg, and varies between 45 and 70 mm Hg. Glomerular capillary pressure is the highest capillary pressure in the body. This pressure favors glomerular filtration.
2. **Colloidal osmotic pressure:** It is the pressure exerted by plasma proteins in the glomeruli. These proteins develop the colloidal osmotic pressure, which is about 25 mm Hg. It opposes glomerular filtration.
3. **Hydrostatic pressure in Bowman capsule:** It is the pressure exerted by the filtrate in Bowman capsule. It is also called **capsular pressure**. It is about 15 mm Hg. It also opposes glomerular filtration.

Net filtration pressure: Net filtration pressure is the balance between pressure favoring filtration and pressures opposing filtration. It is otherwise known as **effective filtration pressure** or **essential filtration pressure**.

$$\text{Net filtration pressure} = 60 - (25 + 15) = 20 \text{ mm Hg.}$$

Starling hypothesis and starling forces: Starling hypothesis states that the net filtration through capillary membrane is proportional to hydrostatic pressure difference across the membrane minus oncotic pressure difference. Hydrostatic pressure within the glomerular capillaries is the glomerular capillary pressure. All the pressures involved in determination of filtration are called **Starling forces**.

Filtration coefficient: It is the GFR per mm Hg of net filtration pressure.

Factors Regulating (Affecting) GFR

1. **Renal blood flow:** GFR is directly proportional to renal blood flow.
2. **Tubuloglomerular feedback:** Tubuloglomerular feedback is the mechanism that regulates GFR through renal tubule and macula densa. **Macula densa** detects the concentration of sodium chloride in the tubular fluid and accordingly alters the glomerular blood flow and GFR. Factors increasing the sensitivity of tubuloglomerular feedback:
 - i. Adenosine
 - ii. Thromboxane
 - iii. Prostaglandin E_2
 - iv. Hydroxyeicosatetranoic acid

Factors decreasing the sensitivity of tubuloglomerular feedback

- i. Atrial natriuretic peptide
- ii. Prostaglandin I_2

iii. Cyclic AMP (cAMP)

iv. Nitrous oxide

When GFR decreases, concentration of sodium chloride decreases in the filtrate. Macula densa secretes prostaglandin (PGE_2), bradykinin and renin. PGE_2 and bradykinin cause dilatation of afferent arteriole. Renin induces the formation of angiotensin II, which causes constriction of efferent arteriole. The dilatation of afferent arteriole and constriction of efferent arteriole leads to increase in glomerular blood flow and GFR.

3. **Glomerular capillary pressure:** Glomerular filtration rate is directly proportional to glomerular capillary pressure.
4. **Colloidal osmotic pressure:** Glomerular filtration rate is inversely proportional to colloidal osmotic pressure.
5. **Hydrostatic pressure in Bowman capsule:** GFR is inversely proportional to this.
6. **Constriction of afferent arteriole:** Constriction of afferent arteriole reduces GFR.
7. **Constriction of efferent arteriole:** Initially the GFR increases because of stagnation of blood in the capillaries. Later when all the substances are filtered from this blood, further filtration does not occur.
8. **Systemic arterial pressure:** Variation in pressure above 180 mm Hg or below 60 mm Hg affects the renal blood flow and GFR accordingly, because the autoregulatory mechanism fails beyond this range.
9. **Sympathetic stimulation:** Initially there is increase in filtration but later it decreases.
10. **Surface area of capillary membrane:** GFR is directly proportional to the surface area of the capillary membrane.
11. **Permeability of capillary membrane:** GFR is directly proportional to the permeability of glomerular capillary membrane.
12. **Contraction of glomerular mesangial cells:** Contraction of these cells decreases surface area of capillaries resulting in reduction in GFR.
13. **Hormonal and other factors:** Factors increasing GFR by vasodilatation (i) atrial natriuretic peptide, (ii) brain natriuretic peptide, (iii) cAMP, (iv) dopamine, (v) endothelial derived nitric oxide, and (vi) Prostaglandin E_2 (PGE_2).

Factors Decreasing GFR by Vasoconstriction

- i. Angiotensin II
- ii. Endothelins
- iii. Noradrenaline
- iv. Platelet activating factor

v. Platelet derived growth factor.

vi. Prostaglandin F_2 (PGF_2)

Q. 3. Define tubular maximum for glucose (TMG). What is the normal value? Mention the other substances which have tubular maximum.

(TNMGR, Oct. 2003)

Ans. Tubular transport maximum or T_m is the rate at which the maximum amount of a substance is reabsorbed from the renal tubule. So, for every actively reabsorbed substance, there is a maximum rate at which it could be reabsorbed. For example, the transport maximum for glucose (T_mG) is 375 mg/minute in adult males and about 300 mg/minute in adult females.

Threshold level in plasma for substances having T_m value: Renal threshold is the plasma concentration at which a substance appears in urine. Every substance having T_m value has also a threshold level in plasma or blood. Below that threshold level, the substance is completely reabsorbed and does not appear in urine. When the concentration of that substance reaches the threshold, the excess amount is not reabsorbed and, so it appears in urine. This level is called the renal threshold of that substance. For example, the renal threshold for glucose is 180 mg/dl. That is, glucose is completely reabsorbed from tubular fluid if its concentration in blood is below 180 mg/dl. So, the glucose does not appear in urine. When the blood level of glucose reaches 180 mg/dl it is not reabsorbed completely; hence it appears in urine.

Q. 4. Write a note on renin-angiotensin system.

(RGUHS, May 2011)

Ans. When renin is released into the blood, it acts on a specific plasma protein called angiotensinogen or renin substrate (α_2 -globulin), converting it into a decapeptide called angiotensin I. Angiotensin I is converted into angiotensin II, which is an **octapeptide** by the activity of **angiotensin-converting enzyme** (ACE) secreted from lungs. Angiotensin II is rapidly degraded into a **heptapeptide** called angiotensin III by **angiotensinases**, which are present in RBCs and vascular beds in many tissues. Angiotensin III is converted into angiotensin IV, which is a **hexapeptide**.

Actions of Angiotensins

1. **Angiotensin I:** Angiotensin I is physiologically inactive and serves only as the precursor of angiotensin II.
2. **Angiotensin II:** Angiotensin II is the most active form. Its actions are given as follows:

On blood vessels

- i. Angiotensin II increases arterial blood pressure by directly acting on the blood vessels and causing vasoconstriction.
- ii. It increases blood pressure indirectly by increasing the release of noradrenaline from postganglionic sympathetic fibers.

On adrenal cortex: It stimulates zona glomerulosa of adrenal cortex to secrete aldosterone. Aldosterone acts on renal tubules and increases retention of sodium, which is also responsible for elevation of blood pressure.

On kidney

- i. Angiotensin II regulates glomerular filtration rate by two ways
 - a. It constricts the efferent arteriole, which causes decrease in filtration after an initial increase.
 - b. It contracts the glomerular mesangial cells leading to decrease in surface area of glomerular capillaries and filtration.
- ii. It increases sodium reabsorption from renal tubules.

On brain

- i. Angiotensin II inhibits the **baroreceptor reflex** and thereby indirectly increases the blood pressure.
- ii. It increases water intake by stimulating the thirst center.
- iii. It increases the secretion of corticotropin-releasing hormone (CRH) from hypothalamus. CRH, in turn, increases secretion of adrenocorticotrophic hormone (ACTH) from pituitary.
- iv. It increases secretion of antidiuretic hormone (ADH) from hypothalamus.

Other actions: Angiotensin II acts as a growth factor in heart and it is thought to cause muscular hypertrophy and cardiac enlargement.

Angiotensin III: Angiotensin III increases the blood pressure and stimulates aldosterone secretion from adrenal cortex.

Angiotensin IV: It also has adrenocortical stimulating and vasopressor activities.

8. CENTRAL NERVOUS SYSTEM

Q. 1. Describe the mechanism of conduction of nerve impulse. (TNMGR, March 2007; BFUHS, Nov. 2011)

Ans. Electrical conductivity is the ability of nerve fibers to transmit the impulse from the area of stimulation to

the other areas. Action potential is transmitted through the nerve fiber as nerve impulse.

Mechanism of conduction of action potential: Depolarization occurs first at the site of stimulation in the nerve fiber. It causes depolarization of the neighboring areas. Like this, depolarization travels throughout the nerve fiber. Depolarization is followed by repolarization.

Conduction through myelinated nerve fiber—saltatory conduction: Saltatory conduction is the form of conduction of nerve impulse in which, the impulse jumps from one node to another. Conduction of impulse through a myelinated nerve fiber is about 50 times faster than through a nonmyelinated fiber.

Mechanism of saltatory conduction: Myelin sheath is not permeable to ions. So, the entry of sodium from extracellular fluid into nerve fiber occurs only in the node of Ranvier, where the myelin sheath is absent. It causes depolarization in the node and not in the internode. Thus, depolarization occurs at successive nodes. So, the action potential jumps from one node to another. Hence, it is called saltatory conduction (saltare = jumping).

Q. 2. Write about molecular mechanism of muscle contraction. (KUHS, Jan., 2014)

Q. What is meant by excitation-contraction coupling? Explain the mechanism. (TNMGR, Oct. 2003)

Ans. It includes three stages:

1. **Excitation-contraction coupling:** The process that occurs in between the excitation and contraction of the muscle. When a muscle is excited (stimulated) by the impulses, action potential is generated in the muscle fiber, which spreads over sarcolemma and also into the muscle fiber through the 'T' tubules. When the action potential reaches the cisternae of 'L' tubules, these cisternae are excited, releasing calcium ions. The calcium ions move towards the actin filaments to produce the contraction.
2. **Role of troponin and tropomyosin:** Large number of calcium ions, which are released from 'L' tubules during the excitation of the muscle, bind with troponin C. It in turn, pulls tropomyosin molecule away from F actin, exposing the active site of F actin. Immediately the head of myosin gets attached to the actin.
3. **Sliding mechanism and formation of actomyosin complex (sliding theory):** It is also called **Ratchet theory** or **Walk along theory**. After binding with active site of F actin, the myosin head is tilted

towards the arm so that the actin filament is dragged along with it. The head immediately breaks away from the active site and returns to the original position. Now, it combines with a new active site on the actin molecule, and the tilting movement occurs again. So, the actin filaments of opposite sides overlap and form actomyosin complex. Formation of actomyosin complex results in contraction of the muscle.

Q. 3. Describe the physiology of pain.

(MUHS, June 2010; BFUHS, Oct. 2010; TNMGR, Oct. 2012)

Q. Discuss the types, properties, pathways and mechanism of pain.

(TNMGR, Feb. 2005; March 2010; April 2013; RGUHS, Oct. 2010)

Q. Write a short note on orofacial pain.

(TNMGR, Sept. 2008; MUHS, June 2010)

Q. Write a note on pathway of dental pain.

(TNMGR, April 1995)

Ans. Pain is defined as “an unpleasant and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.”

Benefits of pain sensation: It provides protective or survival benefits such as:

1. Pain gives warning signal about the existence of a problem or threat. It also creates awareness of injury.
2. Pain prevents further damage by causing reflex withdrawal of the body from the source of injury.
3. Pain forces the person to rest or to minimize the activities thus enabling rapid healing of injured part
4. Pain urges the person to take required treatment to prevent major damage.

Components of pain sensation: Pain sensation has two components—**fast pain** is the first sensation whenever a pain stimulus is applied. It is experienced as a bright, sharp and localized pain sensation. Fast pain is followed by the **slow pain**, which is experienced as a dull, diffused and unpleasant pain. Fast pain sensation is carried by A δ fibers and slow pain sensation is carried by C type of nerve fibers.

Pathways of Pain Sensation (TNMGR, October 2012)

Pain sensation from various parts of body is carried to brain by different pathways which are:

1. **From skin and deeper structures:** Receptors of pain sensation are the free nerve endings, which are distributed throughout the body (Fig. 3.4).

First order neurons: First order neurons are the cells in posterior nerve root ganglia, which receive the impulses of pain sensation from pain receptors through their dendrites. These impulses are transmitted to spinal cord through the axons of these neurons.

- a. **Fast pain fibers:** Fast pain sensation is carried by A δ type afferent fibers which synapse with neurons of marginal nucleus in the posterior gray horn.
- b. **Slow pain fibers:** Slow pain sensation is carried by C type afferent fibers, which synapse with neurons of substantia gelatinosa of Rolando in the posterior gray horn.

Second order neurons: Neurons of marginal nucleus and substantia gelatinosa of Rolando form the second order neurons. Fibers from these neurons ascend in the form of the lateral spinothalamic tract.

- a. **Fast pain fibers:** Fibers of fast pain arise from neurons of marginal nucleus. Immediately after taking origin, the fibers cross the midline via anterior gray commissure, reach the lateral white column of the opposite side and ascend. These fibers form the neospinothalamic fibers in lateral spinothalamic tract. These nerve fibers terminate in ventral posterolateral nucleus of thalamus. Some of the fibers terminate in ascending reticular activating system of brainstem.
- b. **Slow pain fibers:** Fibers of slow pain, which arise from neurons of substantia gelatinosa, cross the midline and run along the fibers of fast pain as paleospinothalamic fibers in lateral spinothalamic tract. One fifth of these fibers terminate in ventral posterolateral nucleus of thalamus. Remaining fibers terminate in any of the following areas:

- i. Nuclei of reticular formation in brainstem.
- ii. Tectum of midbrain.
- iii. Gray matter surrounding aqueduct of Sylvius.

Third order neurons: Third order neurons of pain pathway are the neurons in:

- i. Thalamic nucleus.
- ii. Reticular formation.
- iii. Tectum.
- iv. Gray matter around aqueduct of Sylvius.

Axons from these neurons reach the sensory area of cerebral cortex. Some fibers from reticular formation reach hypothalamus.

Center for pain sensation: Center for pain sensation is in postcentral gyrus of parietal cortex. Fibers reaching hypothalamus are concerned with arousal mechanism due to pain stimulus.

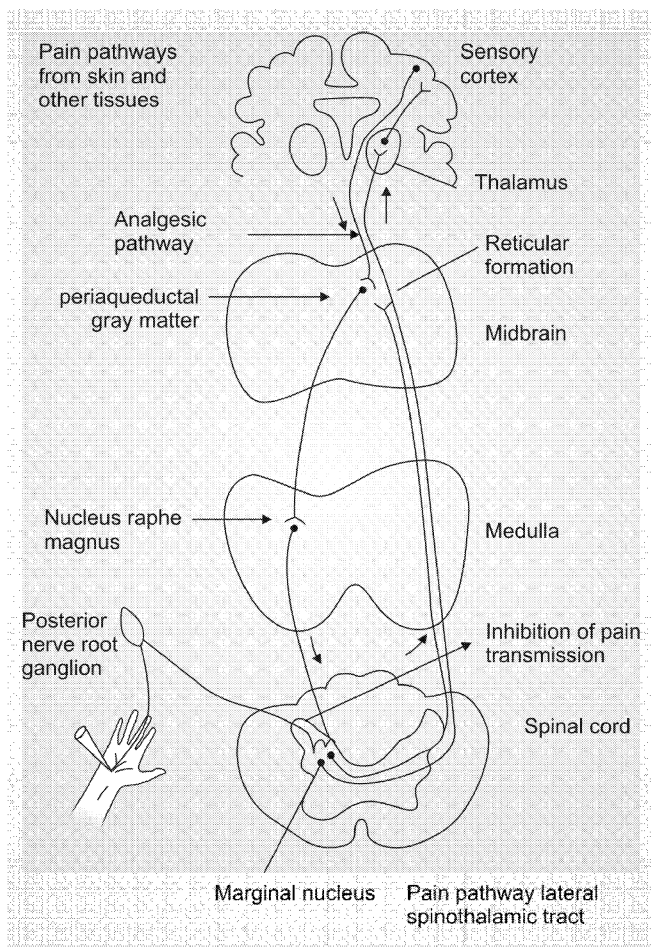


Fig. 3.4: Pain pathway from skin and other deeper structures

2. **From face:** Pain sensation from face is carried by trigeminal nerve (Fig. 3.5).

Pain perception: It is the physioanatomical process by which pain is received and transmitted by neural structures from the end organs or pain receptors, through the conductive and perceptive mechanism.

Pain reaction: It represents the individual's manifestation of unpleasant reaction and involves complex neuroanatomical and psychological factors. Nociceptors are receptors sensitive to noxious stimuli. These are the free nerve endings mostly of myelinated fibers. These are found in orofacial skin, oral mucosa, TMJ, peridontium, tooth pulp, periosteum, muscles, etc. These nociceptors are attached to first order neurons of afferents. The two major classes of afferent nerves that provide input to brain are:

1. **A δ fibers:** large, myelinated, mechanothermal, nociceptive afferent. They respond to intense thermal, mechanical stimuli. They conduct pain fast or first which is sharp and localized.

2. **C fibers:** Small, polymodal, unmyelinated nociceptive afferents. They get excited by strong mechanical, thermal, chemical stimuli. They conduct slow/second pain.

Pain pathways: Pain detection and transmission is done in the orofacial region chiefly by fibers of trigeminal nerve.

1. **Ophthalmic division:** Skin of parietal, frontal region, eyes, nose, orbit and upper part of nasal cavity.
2. **Maxillary division:** Anterior portion of temple, malar, maxillary and nasal cavity, palate, maxillary sinus, and maxillary teeth and gums.
3. **Mandibular division:** Posterior temple, tragus, preauricular area, masseter area, mandibular region, anterior two-thirds of tongue, mandibular teeth and gums, masticatory muscles, tensor muscles of soft palate and tympanic membrane.
4. **Upper second and third cervical nerves:** Superficial structures of head and neck posterior to trigeminal area and below the lower border of mandible and cervical area.
5. **Facial nerve:** Facial skin in mastoid region and external auditory meatus.
6. **Glossopharyngeal nerve:** Posterior part of tongue, tonsillar region, tympanic cavity and antrum.

Transmission of impulses in the CNS: Nerves supplying facial and oral tissues carry information of pain through semilunar or gasserian ganglion, where primary afferent cell bodies are located. From the ganglion, the impulse is mediated by the sensory root of the nerve into pons. Here the sensory root either ends directly in the main sensory nucleus or bifurcates into ascending and descending fibers. The ascending fibers convey general tactile sensibility, whereas the descending fibers convey pain and temperature. Thus, the pain impulse descends from the pons by the spinal tract fibers of the trigeminal nerve, through the medulla, down to the level of second cervical segment, where the tract terminates. The mandibular, maxillary and ophthalmic branches terminate in the nucleus in that order. Axons of the secondary neurons emerge from the spinal nucleus, cross the midline and ascend to join with fibers of the mesencephalic nucleus to form the trigeminal lemniscus or spinothalamic tracts of the 5th nerve. These tracts continue upward and terminate in the posteroventral nucleus of the thalamus. The pain impulse on reaching the posteroventral nucleus of the thalamus is mediated by secondary connecting neurons that projects from the posteroventral thalamus to the posterocentral convolutions of the cerebral cortex. Once the impulse reaches the

thalamus, it is sent to sensory cortex and limbic structure and hypothalamus. The sensory cortex recognizes impulse as pain. Damage to tissues results in release of certain neurochemicals, which play a role in nociception. In chronic pain, sensitization appears to occur at both the peripheral and central nervous system levels. In the peripheral sensitization of trigeminal nerves, small A δ fibers and C-fibers nociceptors become chronically hyperactive to all stimuli

3. **From viscera:** Pain sensation from thoracic and abdominal viscera is transmitted by sympathetic (thoracolumbar) nerves. Pain from esophagus, trachea and pharynx is carried by vagus and glossopharyngeal nerves.
4. **From pelvic region:** Pain sensation from deeper structures of pelvic region is conveyed by sacral parasympathetic nerves.

Visceral pain: Pain from viscera is unpleasant. It is poorly localized.

Causes of visceral pain

1. Ischemia
2. Chemical stimuli
3. Spasm and over-distension of hollow organs.

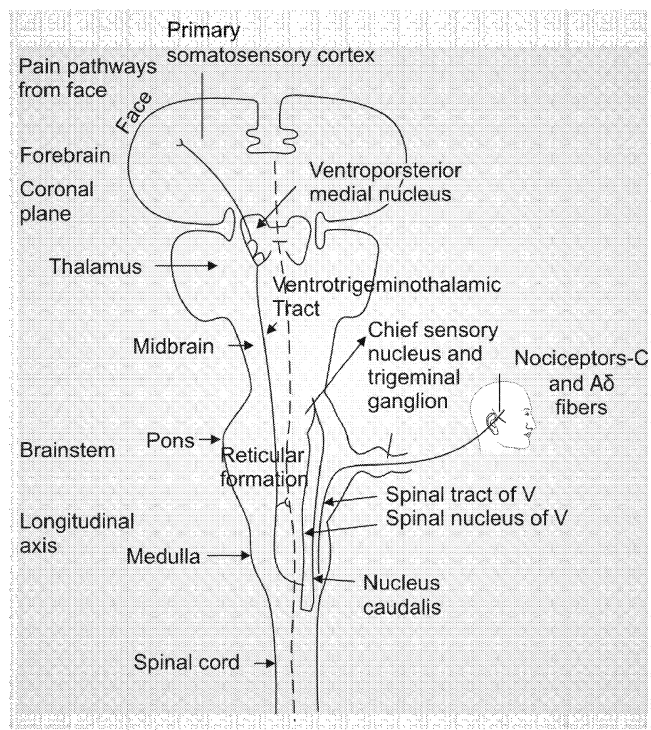


Fig. 3.5: Pain pathway from maxillofacial structures

Q. 4. Define and write about mechanism of referred pain.
(TNMGR, Nov.1995; Oct. 1996)

Q. Write about the physiology of referred pain.

(TNMGR, April 2000, 2012; Oct. 2011)

Ans. Referred pain is the pain that is perceived at a site adjacent to or away from the site of origin. Deep pain and some visceral pain are referred to other areas. But, superficial pain is not referred.

Examples of Referred Pain

1. Cardiac pain is felt at inner part of left arm and left shoulder.
2. Pain in ovary is referred to umbilicus.
3. Pain from testis is felt in abdomen.
4. Pain in diaphragm is referred to shoulder.
5. Pain in gallbladder is referred to epigastric region.
6. Renal pain is referred to loin.

Mechanism of Referred Pain

Dermatome rule: According to dermatome rule, pain is referred to a structure, which is developed from the same dermatome from which the pain producing structure is developed. A dermatome includes all the structures or parts of the body, which are innervated by afferent nerve fibers of one dorsal root. For example, the heart and inner aspect of left arm originate from the same dermatome. So, the pain in heart is referred to left arm.

Neurotransmitters involved in pain sensation:

Glutamate and substance-P are the neurotransmitters secreted by pain nerve endings. A δ afferent fibers, which transmit impulses of fast pain, secrete glutamate. The C type fibers, which transmit impulses of slow pain, secrete substance P.

Analgesia system: Analgesia system means the pain control system. Body has its own analgesia system in brain, which provides a short-term relief from pain. It is also called endogenous analgesic system. Analgesia system has got its own pathway through which it blocks the synaptic transmission of pain sensation in spinal cord and thus attenuates the experience of pain. Analgesic pathway that interferes with pain transmission is often considered as descending pain pathway, the ascending pain pathway being the afferent fibers that transmit pain sensation to the brain.

Role of Analgesic Pathway in Inhibiting Pain Transmission

1. Fibers of analgesic pathway arise from frontal lobe of cerebral cortex and hypothalamus.
2. These fibers terminate in the gray matter surrounding the third ventricle and aqueduct of Sylvius (periaqueductal gray matter).

3. Fibers from here descend down to brainstem and terminate on:
 - i. Nucleus raphe magnus, situated in reticular formation of lower pons and upper medulla.
 - ii. Nucleus reticularis, paragigantocellularis situated in medulla.
4. Fibers from these reticular nuclei descend through lateral white column of spinal cord and reach the synapses of the neurons in afferent pain pathway situated in anterior gray horn. Synapses of the afferent pain pathway are between:
 - i. A δ type afferent fibers and neurons of marginal nucleus.
 - ii. C type afferent fibers and neurons of substantia gelatinosa of Rolando.
5. At synaptic level, analgesic fibers release neurotransmitters and inhibit the pain transmission before being relayed to brain.

Neurotransmitters of analgesic pathway: Neurotransmitters released by the fibers of analgesic pathway are serotonin and opiate receptor substances, namely enkephalin, dynorphin and endorphin.

Q. 5. Elaborate on theories of pain and mode of action of local anesthetics.

(TNMGR, March 2009; Oct. 2013; RGUHS, Oct. 2010)

Ans.

1. **Specific theory:** Given by Descartes in 1644. He considered the pain system as a straight through channel from the skin to the brain. Later Muller postulated the theory of information transmission only by the way of the sensory nerves. Von Frey described specific cutaneous receptors, free nerve endings, for the mediation of touch, heat, cold and pain. A pain center was thought to exist within the brain, which was responsible for all overt manifestations of the unpleasant experience.
2. **Pattern theory:** This theory was proposed by Goldscheider in 1894. This theory suggested that particular patterns of the nerve impulses that evoke pain are produced by summation of sensory input within the dorsal horn of the spinal column. Pain results when the total output of the cells exceeds a critical level.
3. **Gate control theory:** Psychologist Ronald Melzack and the anatomist Patrick Wall proposed the gate control theory for pain in 1965 to explain the pain suppression. According to them, the pain stimuli transmitted by afferent pain fibers are blocked by gate mechanism. Pain pathway and analgesic pathway located at the posterior gray horn of spinal

cord. If the gate is opened, pain is felt. If the gate is closed, pain is suppressed.

Mechanism of Gate Control at Spinal Level

1. When pain stimulus is applied on any part of body, besides pain receptors, the receptors of other sensations such as touch are also stimulated.
2. When all these impulses reach the spinal cord through posterior nerve root, the fibers of touch sensation (posterior column fibers) send collaterals to the neurons of pain pathway, i.e. cells of marginal nucleus and substantia gelatinosa.
3. Impulses of touch sensation passing through these collaterals inhibit the release of glutamate and substance P from the pain fibers.
4. This closes the gate and the pain transmission is blocked.

Role of brain in gate control mechanism: According to Melzack and Wall, brain also plays some important role in the gate control system of the spinal cord as follows:

1. If the gates in spinal cord are not closed, pain signals reach thalamus through lateral spinothalamic tract
2. These signals are processed in thalamus and sent to sensory cortex

Q. 6. Write a note on visual pathway.

(TNMGR, April 2001)

Ans. Visual pathway or optic pathway is the nervous pathway that transmits impulses from retina visual center in cerebral cortex.

Visual receptors: Rods and cones fibers from the visual receptors synapse with dendrites of bipolar cells of inner nuclear layer of the retina.

First order neurons: First order neurons (primary neurons) are **bipolar cells** in the retina. Axons from the bipolar cells synapse with dendrites of ganglionic cells.

Second order neurons: Second order neurons (secondary neurons) are the **ganglionic cells** in ganglionic cell layer of retina. Axons of the ganglionic cells form optic nerve. Optic nerve leaves the eye and terminates in lateral geniculate body.

Third order neurons: Third order neurons are in the **lateral geniculate body**. Fibers arising from here, reach the visual cortex.

Connections of visual receptors to optic nerve: Two pathways exist between the visual receptors and optic nerve:

1. Private pathway
2. Diffuse pathway

Private pathway: The individual cones in fovea centralis are connected to separate bipolar cells. Each bipolar cell is connected to separate ganglionic cell, namely **midget ganglionic cell**. Thus, individual cone is connected to an individual optic nerve fiber. This type of private pathway is responsible for **visual acuity** and **intensity discrimination**.

Diffuse pathway: A number of cones and rods are connected with a polysynaptic bipolar cell. The bipolar cells are connected to **diffused ganglionic cells**. This type of pathway is present outside the fovea.

Course of visual pathway: Visual pathway consists of six components:

1. Optic nerve
2. Optic chiasma
3. Optic tract
4. Lateral geniculate body
5. Optic radiation
6. Visual cortex

Optic nerve: Optic nerve is formed by the axons of ganglionic cells. Optic nerve leaves the eye through optic disk. The fibers from temporal part of retina are in lateral part of the nerve and carry the impulses from nasal half of visual field of same eye. The fibers from nasal part of retina are in medial part of the nerve and carry the impulses from temporal half of visual field of same eye.

Optic chiasma: Medial fibers of each optic nerve cross the midline and join the uncrossed lateral fibers of opposite side, to form the optic tract. This area of crossing of the optic nerve fibers is called optic chiasma.

Optic tract: Optic tract is formed by uncrossed fibers of optic nerve on the same side and crossed fibers of optic nerve from the opposite side. All the fibers of optic tract run backward, outward and towards the **cerebral peduncle**. While reaching the peduncle, the fibers pass between **tuber cinereum** and **anterior perforated substance**. Then, the fibers turn around the peduncle to reach the **lateral geniculate body** in thalamus. Here, many fibers synapse while a few fibers just pass through this and run towards superior colliculus in midbrain. Fibers from fovea do not enter **superior colliculus**. Some fibers from fovea of each side pass through the optic tract of same side and others through the optic tract of opposite side. Due to crossing of medial fibers in optic chiasma, the left optic tract carries impulses from temporal part of left retina and nasal

part of right retina, i.e. it is responsible for vision in nasal half of left visual field and temporal half of right visual field. The right optic tract contains fibers from nasal half of left retina and temporal half of right retina. It is responsible for vision in temporal half of left visual field and nasal half of right visual field.

Lateral geniculate body: Majority of the fibers of optic tract terminate in lateral geniculate body, which forms the **subcortical center** for visual sensation. From here, the **geniculocalcarine tract** or **optic radiation** arises. This tract is the last relay of visual pathway. Some of the fibers from optic tract do not synapse in lateral geniculate body, but pass through it and terminate in one of the following centers:

- i. **Superior colliculus:** It is concerned with reflex movements of eyeballs and head, in response to optic stimulus.
- ii. **Pretectal nucleus:** It is concerned with light reflexes.
- iii. **Supraoptic nucleus of hypothalamus:** It is concerned with the retinal control of pituitary in animals. But in human, it does not play any important role.

Optic radiation: Fibers from lateral geniculate body pass through **internal capsule** and form optic radiation. The fibers between lateral geniculate body and visual cortex are also called **geniculocalcarine fibers**. Optic radiation ends in visual cortex.

Visual cortex: Primary **cortical center** for vision is called visual cortex, which is located on the medial surface of occipital lobe. It forms the walls and lips of calcarine fissure in medial surface of occipital lobe. There is a definite localization of retinal projections upon visual cortex. In fact, the point to point projection of retina upon visual cortex is well established. The peripheral retinal representation occupies the anterior part of visual cortex. **Macular representation** occupies the posterior part of visual cortex near occipital pole.

Areas of visual cortex and their function: Three areas are present in visual cortex:

- i. Primary visual area (area 17), which is concerned with the perception of visual impulses.
- ii. Secondary visual area or visual association area (area 18), which is concerned with the interpretation of visual impulses.
- iii. Occipital eye field (area 19), which is concerned with the movement of eyes.

Applied Physiology

Injury to any part of optic pathway causes visual defect and the nature of defect depends upon the location and extent of injury. Loss of vision in one visual field is

known as **anopia**. Loss of vision in one half of visual field is called **hemianopia**.

Effects of lesion of optic nerve: Lesion in one optic nerve will cause **total blindness** or anopia in the corresponding visual field. Lesion occurs due to increased **intracranial pressure**.

Effects of lesion of optic chiasma: Nature of defect depends upon the fibers involved:

- i. Pressure on uncrossed lateral fibers by aneurysmal dilatation of carotid artery causes blindness in the temporal part of retina of same side. So, the hemianopia developed is called **left or right nasal hemianopia**.
- ii. If lateral fibers of both sides are affected, the vision is lost in nasal half of both visual fields, causing **binasal hemianopia**.
- iii. Compression of nasal fibers by pituitary tumor causes **bitemporal hemianopia**.

Effects of lesion of optic tract, lateral geniculate body and optic radiation: Lesion of optic tract or lateral geniculate body or optic radiation causes **homonymous hemianopia**. In the right-sided lesion, there is loss of vision in right side of both retina, i.e. in left side of both visual fields—left homonymous hemianopia. In the left-sided lesion, there is loss of vision in left half of retina of both eyes and loss of sight on right half of both visual fields—right homonymous hemianopia.

Effects of lesion of visual cortex: Lesion of upper or lower part of visual cortex leads to inferior or superior homonymous hemianopia.

Q. 7. Write about division of autonomic nervous system. (TNMGR, April 2003)

Ans. Autonomic nervous system (ANS) is primarily concerned with regulation of visceral or vegetative functions of the body. So, it is also called vegetative or involuntary nervous system.

Divisions of ANS

1. Sympathetic division
2. Parasympathetic division

Sympathetic division: Sympathetic division is otherwise called **thoracolumbar outflow** because the preganglionic neurons are situated in lateral gray horns of 12 thoracic and first two lumbar segments of spinal cord. Fibers arising from here are known as **preganglionic fibers**. Preganglionic fibers leave the spinal cord through anterior nerve root and white rami communicantes and terminate in the postganglionic neurons, which are situated in the sympathetic ganglia.

Sympathetic division supplies smooth muscle fibers of all the visceral organs such as blood vessels, heart, lungs, glands, gastrointestinal organs, etc.

Sympathetic ganglia: Ganglia of sympathetic division are classified into three groups:

a. **Paravertebral or sympathetic chain ganglia:** Paravertebral or sympathetic chain ganglia are arranged in a segmental fashion along the anterolateral surface of vertebral column. Ganglia on either side of the spinal cord are connected with each other by longitudinal fibers, to form the **sympathetic chains**. Ganglia of the sympathetic chain (trunk) on each side are divided into four groups:

1. Cervical ganglia

- i. **Superior cervical ganglion:** It is formed by the fusion of upper four cervical ganglia. It receives preganglionic fibers from first thoracic spinal segment (T1). Postganglionic fibers from this ganglion, supply the blood vessels, glands, etc. Superior cervical ganglion also sends some fibers to heart through superior cervical sympathetic nerve and cardiac plexus.
- ii. **Middle cervical ganglion:** It is formed by fifth and sixth cervical ganglia. Preganglionic fibers arise from T1 segment. Postganglionic fibers from here supply the sweat glands, thyroid gland and parathyroid glands. It also sends fibers to heart via middle cervical sympathetic nerve and cardiac plexus.
- iii. **Inferior cervical ganglion:** This ganglion is formed by the fusion of seventh and eighth cervical ganglia. First thoracic ganglion fuses with inferior cervical ganglion, forming **stellate ganglion**. It receives preganglionic fibers from T1 segment. It sends postganglionic fibers to heart through inferior cervical sympathetic nerve and cardiac plexus. Postganglionic fibers also form the plexus around subclavian artery and its branches.

2. **Thoracic ganglia:** There are 12 thoracic ganglia on each side. Thoracic ganglia receive preganglionic fibers from the thoracic segments of spinal cord. Postganglionic fibers from thoracic ganglia are distributed to **visceral organs** in the **thorax and abdomen**.

3. **Lumbar ganglia:** There are 5 lumbar ganglia. Preganglionic fibers for these ganglia arise from first and second lumbar spinal segments (L1 and L2). Postganglionic fibers from these ganglia supply the abdominal and **pelvic organs**.

4. **Sacral ganglia:** There are 5 sacral ganglia, which receive the preganglionic fibers from L1 and L2

segments. Postganglionic fibers from sacral ganglia innervate the **blood vessels** and **sweat glands** in the lower limb.

Below the sacral level, both the sympathetic trunks converge and fuse upon the anterior surface of coccyx and form a terminal swelling. This terminal swelling is known as **coccygeal ganglion**. Unpaired coccygeal ganglion is also called **ganglion impar**. It receives preganglionic fibers from L1 and L2 segments. Postganglionic fibers from here are distributed to the abdominal viscera and pelvic region.

b. *Prevertebral or collateral ganglia*: Prevertebral ganglia are situated in thorax, abdomen and pelvis, in relation to aorta and its branches. Prevertebral ganglia are:

1. Celiac ganglion.
2. Superior mesenteric ganglion.
3. Inferior mesenteric ganglion.

Prevertebral ganglia receive preganglionic fibers from T5 to L2 segments. Postganglionic fibers from these ganglia supply the visceral organs of thorax, abdomen and pelvis.

c. *Terminal or peripheral ganglia*: Terminal ganglia are situated within or close to structures innervated by them. Heart, bronchi, pancreas and urinary bladder are innervated by the terminal ganglia.

Parasympathetic division: Parasympathetic division of ANS is called the **craniosacral outflow**.

Cranial outflow or cranial portion of parasympathetic division: Cranial outflow of parasympathetic division arises from brainstem. It innervates the blood vessels of head and neck and many thoracoabdominal visceral organs. Cranial outflow includes the following cranial nerves:

1. Oculomotor (III) nerve
2. Facial (VII) nerve
3. Glossopharyngeal (IX) nerve
4. Vagus (X) nerve

Preganglionic fibers of these cranial nerves arise from neurons situated at two different levels:

1. Tectal or midbrain outflow (III cranial nerve).
2. Bulbar level or bulbar outflow (VII, IX and X cranial nerves).

Preganglionic fibers reach the postganglionic neurons, situated within the organs or close to the organs innervated by these nerves. Preganglionic fibers are myelinated, but the postganglionic fibers are non-myelinated.

1. **Tectal or midbrain outflow**: Group of cells forming **Edinger-Westphal nucleus** of III cranial nerve gives rise to tectal fibers. Fibers from this nucleus end in ciliary ganglion. Postganglionic fibers supply the sphincter pupillae and ciliary muscle.

2. **Bulbar level or bulbar outflow**: Preganglionic fibers are the fibers of VII, IX and X cranial nerves, which arise from the nuclei present in the medulla oblongata. Fibers of VII cranial nerve supply the lacrimal, nasal, submandibular and sublingual glands. Preganglionic fibers end in sphenopalatine ganglion and submandibular ganglion. Postganglionic fibers from sphenopalatine ganglion supply lacrimal and nasal glands. Postganglionic fibers from submandibular ganglion supply sublingual and submandibular glands. Fibers of IX cranial nerve supply the parotid gland. Preganglionic fibers synapse with neurons of otic ganglion. Postganglionic fibers from otic ganglion supply the parotid gland. Fibers of X cranial nerve supply visceral organs of the body. Preganglionic fibers terminate in the ganglia, which are situated on or near the organs. Postganglionic fibers from the ganglia supply the organs. Vagus nerve supplies almost all the organs in the thorax and abdomen, but not the pelvic organs.

Sacral outflow or sacral portion of parasympathetic division: Sacral outflow of parasympathetic division arises from the sacral segments of spinal cord. It innervates smooth muscles forming the walls of viscera and the glands such as large intestine, liver, spleen, kidneys, bladder, genitalia, etc. Preganglionic fibers arise from anterior gray horn cells of 2nd, 3rd and 4th sacral segments of spinal cord and form the pelvic nerve (**nervi erigens**). Fibers end on postganglionic neurons. Fibers from postganglionic neurons supply descending colon, rectum, urinary bladder, internal sphincter, urethra and accessory sex organs.

Functions of ANS: Autonomic nervous system is concerned with the regulation of functions, which are beyond voluntary control. By controlling the various vegetative functions, ANS plays an important role in maintaining constant internal environment (homeostasis). Almost all the visceral organs are supplied by both sympathetic and parasympathetic divisions of ANS and the two divisions produce antagonistic effects on each organ. When the fibers of one division supplying to an organ is sectioned or affected by lesion, the effects of fibers from other division on the organ become more prominent.

1. CARBOHYDRATES, PROTEINS AND FAT

Q. 1. Write a note on anabolism and catabolism.

(TNMGR, April 2013)

Ans. The entire spectrum of chemical reactions occurring in the living system is collectively referred to as **metabolism**. Metabolism is broadly divided into two categories:

1. **Catabolism:** The degradative processes concerned with the breakdown of complex molecules to simpler ones with a concomitant release of energy. The purpose of catabolism is to trap the energy of the biomolecules in the form of ATP and to generate the substances required for the synthesis of complex molecules. Catabolism occurs in three stages:
 - a. *Conversion of complex molecules into their building blocks:* Polysaccharides are broken down to monosaccharides, lipids to free fatty acids and glycerol, proteins to amino acids.
 - b. *Formation of simple intermediates:* The building blocks produced are degraded to simple intermediates such as pyruvate and acetyl CoA.
 - c. *Final oxidation of acetyl CoA:* Acetyl CoA is completely oxidized to CO_2 , liberating NADH and FADH_2 that finally get oxidized to release large quantity of energy (as ATP). Krebs cycle is the common metabolic pathway involved in the final oxidation of all energy-rich molecules.
2. **Anabolism:** The biosynthetic reactions involving the formation of complex molecules from simple precursors. For the synthesis of a large variety of complex molecules, the starting materials include pyruvate, acetyl CoA and the intermediates of citric acid cycle. Besides the availability of precursors, the anabolic reactions are dependent on the supply of energy (as ATP or GTP) and reducing equivalents (as $\text{NADPH} + \text{H}^+$).

Q. 2. Write a short note on homopolysaccharides.

(TNMGR, April 1997)

Ans. Homopolysaccharides are polysaccharides which on hydrolysis gives only a single type of monosaccharide. They are named based on the nature of the monosaccharide unit. Glucans are polymers of glucose, fructosans are polymers of fructose. The various homopolysaccharides are:

1. **Starch:** Starch is the carbohydrate reserve of plants which is the most important dietary source for higher animals, including man. High content of starch is found in cereals, roots, tubers, vegetables, etc. Starch is a homopolymer composed of D-glucose units held by α -glycosidic bonds. It is known as **glucosan** or **glucan**. Starch consists of two polysaccharide components—water-soluble amylose (15–20%) and a water-insoluble amylopectin (80–85%). Starches are hydrolyzed by amylase to liberate dextrans, and finally maltose and glucose units.
2. **Dextrans:** Dextrans are breakdown products of starch by enzyme amylase. Starch is sequentially hydrolysed through different dextrans and finally to maltose and glucose.
3. **Inulin:** Inulin is a polymer of fructose, fructosan. It is low molecular weight polysaccharides easily soluble in water, used for assessing kidney function.
4. **Glycogen:** It is the carbohydrate reserve in animals, animal starch.
5. **Cellulose:** It occurs exclusively in plants.
6. **Chitin:** It is structural polysaccharide found in the exoskeleton of some invertebrates. It is composed of N-acetyl-D-glucosamine units.

Q. 3. Write a short note on mucopolysaccharides.

(TNMGR, Oct. 1996)

Ans. Mucopolysaccharides are heteroglycans/heteropolysaccharides made up of repeating units of sugar derivatives, namely amino sugars and uronic acids.

These are more commonly known as **glycosaminoglycans** (GAG). Acetylated amino groups, besides sulfate and carboxyl groups are generally present in GAG structure. The presence of sulfate and carboxyl groups contributes to acidity of the molecules, making them acid mucopolysaccharides. Some of the mucopolysaccharides are found in combination with proteins to form mucoproteins or mucoids or proteoglycans. Mucoproteins may contain up to 95% carbohydrate and 5% protein. Mucopolysaccharides are essential components of tissue structure. The extracellular spaces of tissue (particularly connective tissue—cartilage, skin, blood vessels, tendons) consist of collagen and elastin fibers embedded in a matrix or ground substance. The ground substance is predominantly composed of GAG. The important mucopolysaccharides include hyaluronic acid, chondroitin 4-sulfate, heparin, dermatan sulfate and keratan sulfate.

Q. 4. Write a note on carbohydrate metabolism.

(TNMGR, March 2010)

Ans. Carbohydrates are the first cellular constituents synthesized by green plants during photosynthesis from carbon dioxide and water, on absorption of light. The monosaccharide, glucose is the central molecule in carbohydrate metabolism since all the major pathways of carbohydrate metabolism are connected with it. Glucose is utilized as a source of energy, it is synthesized from non-carbohydrate precursors and stored as glycogen to release glucose as and when the need arises. The other monosaccharides important in carbohydrate metabolism are fructose, galactose and mannose. The fasting blood glucose level in normal individuals is 70–100 mg/dl (4.5–5.5 mmol/L). Liver plays a key role in monitoring and stabilizing blood glucose levels. Thus, liver may be appropriately considered as glucostat monitor. The important pathways of carbohydrate metabolism are:

1. **Glycolysis (Embden-Meyerhof pathway):** The oxidation of glucose to pyruvate and lactate.
2. **Citric acid cycle (Krebs cycle or tricarboxylic acid cycle):** The oxidation of acetyl CoA to CO₂. Krebs cycle is the final common oxidative pathway for carbohydrates, fats or amino acids, through acetyl CoA.
3. **Gluconeogenesis:** The synthesis of glucose from non-carbohydrate precursors (e.g. amino acids, glycerol etc.).
4. **Glycogenesis:** The formation of glycogen from glucose.

5. **Glycogenolysis:** The breakdown of glycogen to glucose.
6. **Hexose monophosphate shunt (pentose phosphate pathway or direct oxidative pathway):** This pathway is an alternative to glycolysis and TCA cycle for the oxidation of glucose (directly to carbon dioxide and water).
7. **Uronic acid pathway:** Glucose is converted to glucuronic acid, pentoses, and in some animals to ascorbic acid (not in man). This pathway is also an alternative oxidative pathway for glucose.
8. **Galactose metabolism:** The pathways concerned with the conversion of galactose to glucose and the synthesis of lactose.
9. **Fructose metabolism:** The oxidation of fructose to pyruvate and the relation between fructose and glucose metabolism.
10. **Amino sugar and mucopolysaccharide metabolism:** The synthesis of amino sugars and other sugars for the formation of mucopolysaccharides and glycoproteins.

Q. 5. Discuss glycolytic pathways. (RGUHS, May 2011)

Q. Write a note on anaerobic glycolysis.

(TNMGR, April 1998)

Q. Discuss glucose metabolism, diabetes mellitus and the clinical implication in the management of a patient with diabetes. (Pacific Uni., May 2010)

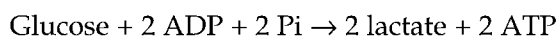
Q. Write a short note on metabolism of sucrose.

(TNMGR, Sept. 2007)

Ans. **Glycolysis/Embden-Meyerhof pathway** (EM pathway) is defined as the sequence of reactions converting glucose (or glycogen) to pyruvate or lactate, with the production of ATP.

Salient Features

1. Glycolysis takes place in all cells of the body.
2. Glycolysis occurs in the absence of oxygen (anaerobic) or in the presence of oxygen (aerobic). Lactate is the end product under anaerobic condition. In the aerobic condition, pyruvate is formed, which is then oxidized to CO₂ and H₂O.
3. Glycolysis is a major pathway for ATP synthesis in tissues lacking mitochondria, e.g. erythrocytes, cornea, lens, etc.
4. Glycolysis is very essential for brain which is dependent on glucose for energy.
5. Glycolysis (anaerobic) may be summarized by the net reaction



The pathway can be divided into three distinct phases

a. Energy investment phase or priming stage

1. Glucose is phosphorylated to glucose 6-phosphate by hexokinase or glucokinase.
2. Glucose-6-phosphate undergoes isomerization to fructose-6-phosphate by phosphohexose isomerase.
3. Fructose-6-phosphate is phosphorylated to fructose-1, 6-bisphosphate by phosphofructokinase.

b. Splitting phase

1. Fructose-1, 6-bisphosphate is split by aldolase into glyceraldehyde 3-phosphate and dihydroxyacetone phosphate.

c. Energy generation phase

1. Glyceraldehyde-3-phosphate is converted into 1,3-bisphosphoglycerate by glyceraldehyde-3-phosphate dehydrogenase.
2. 1,3-bisphosphoglycerate is converted to 3-phosphoglycerate by phosphoglycerate kinase.
3. 3-phosphoglycerate is converted to 2-phosphoglycerate by phosphoglycerate mutase.
4. 2-phosphoglycerate is converted to phosphoenolpyruvate by enolase.
5. Phosphoenolpyruvate is converted to pyruvate by pyruvate kinase, further lactate dehydrogenase converts pyruvate into lactate.

Production of ATP

1. Under anaerobic condition: 2 ATP.
2. Under aerobic condition: 6/8 ATP.

Regulation of glycolysis: Enzymes, namely hexokinase (and glucokinase), phosphofructokinase and pyruvate kinase, catalysing the irreversible reactions regulate glycolysis.

Diabetes mellitus: Diabetes mellitus is a clinical condition characterized by increased blood glucose level (hyperglycemia) due to insufficient or inefficient (incompetent) insulin. As a consequence the blood glucose level is elevated which spills over into urine in diabetes mellitus.

Metabolic changes in diabetes: Diabetes mellitus is associated with several metabolic alterations. Most important among them are:

1. **Hyperglycemia:** Elevation of blood glucose concentration is the hallmark of uncontrolled diabetes. Hyperglycemia is primarily due to reduced glucose uptake by tissues and its increased production via gluconeogenesis and glycogenolysis. When the blood glucose level goes beyond the renal threshold, glucose is excreted into urine (glycosuria).

2. **Ketoacidosis:** Increased mobilization of fatty acids results in overproduction of ketone bodies which often leads to ketoacidosis.
3. **Hypertriglyceridemia:** Conversion of fatty acids to triacylglycerols and the secretion of VLDL and chylomicrons is comparatively higher in diabetics. Further, the activity of the enzyme lipoprotein lipase is low in diabetic patients. Consequently, the plasma levels of VLDL, chylomicrons and triacylglycerols are increased. Hypercholesterolemia is also frequently seen in diabetics.

Long-term effects: Hyperglycemia is directly or indirectly associated with several complications. These include atherosclerosis, retinopathy, nephropathy and neuropathy. The biochemical basis of these complications is not clearly understood. It is believed that at least some of them are related to microvascular changes caused by glycation of proteins.

Management of Diabetes

1. **Dietary management:** A diabetic patient is advised to consume low calories (i.e. low carbohydrate and fat), high protein and fiber-rich diet. Diet control and exercise will help to a large extent obese non-insulin dependent diabetes mellitus (NIDDM) patients.
2. **Hypoglycemic drugs:** They promote the secretion of endogenous insulin and thus help in reducing blood glucose level.
3. **Management with insulin:** The short-acting insulins are unmodified and their action lasts for about 6 hours. The long-acting insulins are modified ones (such as adsorption to protamine) and act for several hours, which depends on the type of preparation.

Q. 6. Write short notes on oxidative phosphorylation.
(TNMGR, Oct. 1999)

Ans. The process of synthesizing ATP from ADP and P_i coupled with the electron transport chain (ETC) is known as oxidative phosphorylation. The inner mitochondrial membrane is the site of oxidative phosphorylation.

P:O ratio: The P:O ratio refers to the number of inorganic phosphate molecules utilized for ATP generation for every atom of oxygen consumed. P:O ratio represents the number of molecules of ATP synthesized per pair of electrons carried through ETC. The mitochondrial oxidation of NADH has P:O ratio of 3. Oxidation of $FADH_2$ has a P:O ratio of 2.

Sites of oxidative phosphorylation in ETC: There are three reactions in the ETC that are exergonic to result in the synthesis of 3 ATP molecules.

1. Oxidation of FMN H_2 by coenzyme Q
2. Oxidation of cytochrome b by cytochrome C₁
3. Cytochrome oxidase reaction

Mechanism of Oxidative Phosphorylation

1. **Chemical coupling hypothesis:** According to this hypothesis, during the course of electron transfer in respiratory chain, a series of phosphorylated high-energy intermediates are first produced which are utilized for the synthesis of ATP.
2. **Chemiosmotic hypothesis:** This mechanism is now widely accepted. The inner mitochondrial membrane is impermeable to protons (H^+) and hydroxyl ions (OH^-). The transport of electrons through ETC is coupled with the translocation of protons (H^+) across the inner mitochondrial membrane (coupling membrane) from the matrix to the intermembrane space. The proton gradient developed due to the electron flow in the respiratory chain is sufficient to result in the synthesis of ATP from ADP and Pi. Also the ATP synthase, utilizes the proton gradient for the synthesis of ATP. This enzyme is also known as ATPase.

Q. 7. Write a short note on ketone bodies.

Ans. Acetone, acetoacetate and β -hydroxybutyrate are the ketone bodies.

Ketogenesis: The synthesis of ketone bodies occurs in the liver. The enzymes for ketone body synthesis are located in the mitochondrial matrix. Acetyl CoA is the precursor for ketone bodies. Ketogenesis occurs through the following reaction:

1. Two moles of acetyl CoA condense to form acetoacetyl CoA. This reaction is catalyzed by thiolase, an enzyme involved in the final step of β -oxidation.
2. Acetoacetyl CoA combines with another molecule of acetyl CoA to produce β -hydroxy β -methyl glutaryl CoA (HMG CoA). HMG CoA synthase, catalyzing this reaction, regulates the synthesis of ketone bodies.
3. HMG CoA lyase cleaves HMG CoA to produce acetoacetate and acetyl CoA.
4. Acetoacetate can undergo spontaneous decarboxylation to form acetone.
5. Acetoacetate can be reduced by a dehydrogenase to β -hydroxybutyrate.

The carbon skeleton of some amino acids (ketogenic) is degraded to acetoacetate or acetyl CoA, and therefore to ketone bodies, e.g. leucine, lysine, phenylalanine, etc.

Utilization: Ketone bodies being water-soluble are easily transported from the liver to various tissues. The

two ketone bodies—acetoacetate and β -hydroxybutyrate serve as important sources of energy for the peripheral tissues such as skeletal muscle, cardiac muscle/renal cortex, etc. The tissues which lack mitochondria (e.g. erythrocytes) cannot utilize ketone bodies. During prolonged starvation, ketone bodies are the major fuel source for brain and other parts of central nervous system. The overproduction of ketone bodies leads to ketonemia followed by ketonuria and ultimately ketosis.

Regulation

1. Glucagon stimulates the ketogenesis.
2. Insulin inhibits ketogenesis.

Ketogenic substance: Fatty acids and amino acids.

Antiketogenic substance: Glucose, glycerol, glucogenic amino acids.

Q. 8. Write a short note on gluconeogenesis.

(TNMGR, March 2009)

Ans. The synthesis of glucose from non-carbohydrate compounds is known as gluconeogenesis.

The major substrates for gluconeogenesis are lactate, pyruvate, glucogenic amino acids, propionate and glycerol.

Location of gluconeogenesis: Gluconeogenesis occurs mainly in the cytosol, mostly in liver and in kidney matrix.

Importance: Glucose occupies a key position in the metabolism and its continuous supply is absolutely essential for the body for a variety of functions:

1. Brain and central nervous system/erythrocytes, testes and medulla of kidney are dependent on glucose for continuous supply of energy.
2. Glucose is the only source that supplies energy to the skeletal muscle, under anaerobic conditions.
3. In fasting, gluconeogenesis must occur to meet the basal requirements of the body for glucose and to maintain the intermediates of citric acid cycle.
4. Certain metabolites produced in the tissues accumulate in the blood, e.g. lactate, glycerol, propionate, etc. Gluconeogenesis effectively clears them from the blood.

Gluconeogenesis closely resembles the reversed pathway of glycolysis, although it is not the complete reversal of glycolysis. Essentially 3 (out of 10) reactions of glycolysis are irreversible.

1. Conversion of pyruvate to phosphoenol pyruvate.
2. Conversion of fructose-1, 6-bisphosphate to fructose 6-phosphate.
3. Conversion of glucose-6-phosphate to glucose.

The overall summary of gluconeogenesis or the conversion of pyruvate to glucose is shown below.



Regulation of Gluconeogenesis

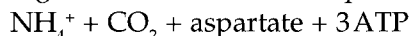
1. Glucagon stimulates gluconeogenesis.
2. Glucogenic amino acids stimulate gluconeogenesis.
3. Acetyl CoA stimulates gluconeogenesis.

Q. 9. Write a note on urea cycle.

(TNMGR, Oct. 2003, Aug. 2004)

Ans. Urea is the end product of protein metabolism. The nitrogen of amino acids converted to ammonia, is toxic to the body. It is converted to urea and detoxified. Urea is synthesized in liver and transported to kidneys for excretion in urine. Urea cycle is known as **Krebs-Henseleit cycle**.

Urea has two amino ($-\text{NH}_2$) groups, one derived from NH_3 and the other from aspartate. Carbon atom is supplied by CO_2 . Urea synthesis is a five-step cyclic process, with five distinct enzymes. The first two enzymes are present in mitochondria while the rest are localized in cytosol. The urea cycle is irreversible and consumes 4 ATP. Two ATPs are utilized for the synthesis of carbamoyl phosphate. One ATP is converted to AMP and PPi to produce argininosuccinate which equals to 2 ATP.



Steps in Urea Formation

1. Carbamoyl phosphate synthase I catalyse the condensation of NH_4^+ with CO_2 to form carbamoyl phosphate.
2. Citrulline is formed from carbamoyl phosphate and ornithine by ornithine transcarbamoylase.
3. Argininosuccinate is formed from citrulline with aspartate by argininosuccinate synthase.
4. Argininosuccinase cleaves argininosuccinate to give arginine and fumarate.
5. Arginase cleaves arginine to yield urea and ornithine.

Q. 10. Write a short note on glycoproteins.

(TNMGR, March 2007)

Ans. Proteins bound to carbohydrates are called glycoproteins. The carbohydrate content varies from 1 to 90%. The term mucoprotein is used when the carbohydrate content is more than 4%. For example, mucin, ovomucoid. The carbohydrate found in glycoproteins include mannose, galactose, N-

acetylglucosamine, N-acetylgalactosamine, xylose, L-fucose and N-acetylneuraminic acid.

Q. 11. Write a short note on lipoproteins.

(TNMGR, April 2012)

Ans. Lipoproteins are molecular complexes of lipids with proteins (conjugated proteins). They are the transport vehicles for lipids in the circulation. A lipoprotein is basically consists of neutral lipid core surrounded by a coat shell of phospholipids, apoproteins and cholesterol. The polar portion of the phospholipids and cholesterol are exposed on the surface of lipoproteins, which makes it soluble with water.

Classification

1. **Chylomicrons:** Synthesized in intestine, consist of highest quantity of lipid, least in density and largest in size, transport exogenous triacylglycerol to tissues.
2. **Very low density lipoproteins (VLDL):** Produced in liver and intestine, responsible for endogenously synthesized triacylglycerols.
3. **Low density lipoproteins (LDL):** Formed from VLDL in the blood circulation, transport cholesterol from liver to other tissues.
4. **High density lipoproteins (HDL):** Mostly synthesized in liver, transport cholesterol from peripheral tissues to liver.
5. **Free fatty acid-albumin complexes:** Each molecule of albumin can hold about 20–30 molecules of free fatty acids.

Disorders of Plasma Lipoproteins

Hyperlipoproteinemias: Elevation in one or more of the lipoprotein fractions constitutes hyperlipoproteinemias.

1. **Type I:** This is due to familial lipoprotein lipase deficiency. The enzyme defect causes increase in plasma chylomicron and triacylglycerol levels.
2. **Type IIa:** This is also known as **hyperbetalipoproteinemia** and is caused by a defect in LDL receptors. Secondary type IIa hyperlipoproteinemia is observed in association with diabetes mellitus, hypothyroidism, nephrotic syndrome, etc. This disorder is characterized by hypercholesterolemia.
3. **Type IIb:** Both LDL and VLDL increase along with elevation in plasma cholesterol and triacylglycerol. This is believed to be due to overproduction of apoprotein B.
4. **Type III:** This is commonly known as broad beta disease and characterized by the appearance of a broad β -band corresponding to intermediate density lipoprotein (IDL) on electrophoresis.

5. *Type IV*: This is due to overproduction of endogenous triacylglycerols with a concomitant rise in VLDL. Type IV disorder is usually associated with obesity, alcoholism, diabetes mellitus, etc.
6. *Type V*: Both chylomicrons and VLDL are elevated. This is mostly a secondary condition, due to disorders such as obesity, diabetes, excessive alcohol consumption, etc.

Hypolipoproteinemias

1. **Familial hypobetalipoproteinemia**: It is an inherited disorder probably due to an impairment in the synthesis of apoprotein B.
2. **Abetalipoproteinemia**: This is a rare disorder due to a defect in the synthesis of apoprotein B. It is characterized by a total absence of β -lipoprotein (LDL) in plasma.

Familial alphasipoprotein deficiency (Tangier disease): The plasma HDL particles are almost absent. Due to this, the reverse transport of cholesterol is severely affected leading to the accumulation of cholesteryl esters in tissues. The affected individuals are at an increased risk for atherosclerosis.

Q. 12. Write a short note on Krebs cycle.

(TNMGR, March 2009; RUHS, May 2015)

Q. Write a short note on citric acid cycle.

(TNMGR, Nov. 1995)

Ans. The citric acid cycle (Krebs cycle or tricarboxylic acid—TCA cycle) is the most important metabolic pathway for the energy supply to the body. Citric acid cycle essentially involves the oxidation of acetyl CoA to CO_2 and H_2O .

TCA cycle—the central metabolic pathway: Krebs cycle is the most important central pathway connecting almost all the individual metabolic pathways (either directly or indirectly).

Reactions of Citric Acid Cycle

1. Condensation of acetyl CoA and oxaloacetate by citrate synthase forms citryl CoA, which yields citrate.
2. Citrate is isomerized to isocitrate by aconitase.
3. Isocitrate is converted to oxalosuccinate then to α -ketoglutarate by isocitrate dehydrogenase.
4. α -ketoglutarate is converted to succinyl CoA by α -ketoglutarate dehydrogenase.
5. Succinyl CoA is converted to succinate by succinate thiokinase.
6. Succinate is converted to fumarate by succinate dehydrogenase.

7. Fumarate is converted to malate by fumarase.
8. Malate is converted to oxaloacetate by malate dehydrogenase.

ATP produced: 12 ATP.

Regulation of cycle: Enzymes citrate synthase, isocitrate dehydrogenase and α -ketoglutarate dehydrogenase.

Q. 13. Write a note on essential amino acids.

(TNMGR, Oct. 2012, 2013)

Ans. They are also known as indispensable amino acids, amino acids which cannot be synthesized by the body, and therefore, need to be supplied through diet are called essential amino acids. They are required for proper growth and maintenance of the individual.

Arginine, valine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan.

Arginine and histidine can be partly synthesized by adult humans, hence, these are considered as **semi-essential amino acids**.

Q. 14. Write a short note on absorption of fat.

(TNMGR, April 1998)

Ans. Theories to explain the absorption of lipids are:

1. **Lipolytic theory**: Fats are completely hydrolysed to glycerol and free fatty acids. The latter are absorbed either as soaps or in association with bile salts.
2. **Partition theory proposed by frazer**: The partially digested triacylglycerols in association with bile salts form emulsions. The lipids are taken up by the intestinal mucosal cells. As per this theory, resynthesis of lipids is not necessary for their entry into the circulation.
3. **Bergstrom theory**: This is a more recent and comprehensive theory to explain lipid absorption. The primary products obtained from the lipid digestion are 2-monoacylglycerol free fatty acids and free cholesterol.

Role of bile salts in lipid absorption: Bile salts form mixed micelles with lipids. The micelles have a disk like shape with lipids at the interior and bile salts at the periphery. The hydrophilic groups of the lipids are oriented to the outside and the hydrophobic groups to the inside. In this fashion, the bile salt micelles exert a solubilizing effect on the lipids. The mixed micelles serve as the major vehicles for the transport of lipids from the intestinal lumen to the membrane of the intestinal mucosal cells, the site of lipid absorption. The lipid components pass through the unstirred fluid layer and are absorbed through the plasma membrane by diffusion. Absorption is almost complete for mono-

acylglycerols and free fatty acids which are slightly water-soluble. However, for water-insoluble lipids, the absorption is incomplete. The efficiency of lipid absorption is dependent on the quantity of bile salts to solubilize digested lipids in the mixed micelles.

Q. 15. Write a note on lipid absorption from intestine.

(TNMGR, March 2007)

Ans. Emulsification (dispersion of lipids into smaller droplets due to reduction in the surface tension) is essential for effective digestion of lipids, since the enzymes can act only on the surface of lipid droplets. The process of emulsification occurs by three complementary mechanisms:

1. **Detergent action of bile salts:** Bile salts convert them into smaller particles.
2. **Surfactant action of degraded lipids:** Surfactants get absorbed to the water-lipid interfaces and increase the interfacial area of lipid droplets.
3. **Mechanical mixing due to peristalsis:** Mechanical mixing due to peristalsis also helps in the emulsification of lipids.

Digestion of lipids by pancreatic enzymes: The pancreatic enzymes are primarily responsible for the degradation of dietary triacylglycerols, cholesteryl esters and phospholipids.

1. **Degradation of triacylglycerols (fat)**
 - a. Pancreatic lipase is the major enzyme that digests dietary fats. This enzyme preferentially cleaves fatty acids, forming 2-monoacylglycerol and free fatty acids.
 - b. Lipid esterase acts on monoacylglycerols, cholesteryl esters, vitamin esters, etc. to liberate free fatty acids. The presence of bile acids is essential for the activity of lipid esterase.
2. **Degradation of cholesteryl esters:** Pancreatic cholesterol esterase (cholesteryl ester hydrolase) cleaves cholesteryl esters to produce cholesterol and free fatty acids.
3. **Degradation of phospholipids:** Phospholipases are enzymes responsible for the hydrolysis of phospholipids. The products are a free fatty acid and a lysophospholipid.

Q. 16. Write a note on β -oxidation of fatty acids.

(TNMGR, Oct. 1996)

Ans. β -oxidation may be defined as the oxidation of fatty acids on the β -carbon atom. This results in the sequential removal of a two-carbon fragment, acetyl CoA. The β -oxidation of fatty acids involves three stages.

- i. **Fatty acid activation:** Fatty acids are activated to acyl CoA by thiokinases or acyl CoA synthetases. The reaction occurs in two steps and requires ATP, coenzyme A and Mg^{2+} .
- ii. **Transport of acyl CoA into mitochondria:** The inner mitochondrial membrane is impermeable to fatty acids. A specialized carnitine carrier system (carnitine shuttle) operates to transport activated fatty acids from cytosol to the mitochondria.
- iii. **β -oxidation proper:** Each cycle of β -oxidation, liberating a two-carbon unit-acetyl CoA, occurs in a sequence of four reactions.
 1. Acyl CoA undergoes dehydrogenation by an FAD-dependent flavoenzyme, acyl CoA dehydrogenase.
 2. Enoyl CoA hydratase brings about the hydration of the double bond to form β -hydroxyacyl CoA.
 3. β -hydroxyacyl CoA dehydrogenase catalyses the second oxidation and generates NADH. The product formed is β -ketoacyl CoA.
 4. The final reaction in β -oxidation is the liberation of a 2-carbon fragment, acetyl CoA from acyl CoA. This occurs by a thiolytic cleavage catalyzed by β -ketoacyl CoA thiolase.

The new acyl CoA, containing two-carbon less than the original, reenters the β -oxidation cycle. The process continues till the fatty acid is completely oxidized. The scheme of fatty acid oxidation discussed above corresponds to saturated and even carbon fatty acids. This occurs most predominantly in biological system.

Oxidation of palmitoyl CoA: Palmitoyl CoA undergoes 7 cycles of β -oxidation to yield 8 acetyl CoA. Acetyl CoA can enter citric acid cycle and get completely oxidized to CO_2 and H_2O .

SIDS—a disorder due to blockade in β -oxidation: The sudden infant death syndrome (SIDS) is an unexpected death of healthy infants, usually overnight. The real cause of SIDS is not known.

It is now estimated that at least 10% of SIDS is due to deficiency of medium chain acyl CoA dehydrogenase.

Jamaican vomiting sickness: This disease is characterized by severe hypoglycemia, vomiting, convulsions, coma and death. It is caused by eating unripe ackee fruit which contains an unusual toxic amino acid, hypoglycin A. This inhibits the enzyme acyl CoA dehydrogenase and thus β -oxidation of fatty acids is blocked, leading to various complications.

Q. 17. Write a short note on cholesterol, its chemistry and functions.

(TNMGR, April 1997, 2000, March 2007)

Ans. Cholesterol is found exclusively in animals, hence it is often called as **animal sterol**. The total body content of cholesterol in an adult man weighing 70 kg is about 140 g, i.e. around 2 g/kg body weight.

Functions

1. It is a structural component of cell membrane.
2. It is the precursor for the synthesis of all other steroids in the body.
3. It is an essential ingredient in the structure of lipoproteins, in which form the lipids in the body are transported.
4. Fatty acids are transported to liver as cholesteryl esters for oxidation.

Cholesterol biosynthesis: All the tissues of the body participate in cholesterol biosynthesis. The largest contribution is made by liver (50%), intestine, skin, adrenal cortex, reproductive tissue, etc. The enzymes involved in cholesterol synthesis are found in the cytosol and microsomal fractions of the cell. Acetate of acetyl CoA provides all the carbon atoms in cholesterol. The reducing equivalents are supplied by NADPH while ATP provides energy. For the production of one mole of cholesterol, 18 moles of acetyl CoA, 36 moles of ATP and 16 moles of NADPH are required. The synthesis of cholesterol occurs in 5 stages:

1. Synthesis of HMG CoA
2. Formation of mevalonate (6C)
3. Production of isoprenoid units (5C)
4. Synthesis of squalene (30C)
5. Conversion of squalene to cholesterol (27C)

Regulation of cholesterol synthesis: Cholesterol biosynthesis is controlled by the rate limiting enzyme HMG CoA reductase at the beginning of the pathway.

1. **Feedback control:** Increase in the cellular concentration of cholesterol reduces the synthesis of the enzyme HMG CoA reductase.
2. **Hormonal regulation:** Glucagon and glucocorticoids decrease cholesterol synthesis. Insulin and thyroxine increase cholesterol production.
3. **Inhibition by drugs:** Compactin and lovastatin reduce cholesterol synthesis.
4. HMG CoA reductase activity is inhibited by bile acids.
5. Fasting also reduces the activity of this enzyme.

Degradation of cholesterol: Cholesterol is converted to bile acids (excreted in feces), serves as a precursor for the synthesis of steroid hormones, vitamin D, coprostanol and cholestanol.

Transport of cholesterol: Cholesterol is present in the plasma lipoproteins in two forms.

1. About 70–75% of it is in an esterified form with long chain fatty acids.
2. About 25–30% as free cholesterol. This form of cholesterol readily exchanges between different lipoproteins and also with the cell membranes.

Clinical importance of serum cholesterol level: In healthy individuals, the total plasma cholesterol is in the range of 150–200 mg/dl. In the newborn, it is less than 100 mg/dl and rises to about 150 mg/dl within an year. The women have relatively lower plasma cholesterol which is attributed to the hormones-estrogens. Cholesterol level increases with increasing age (in women particularly after menopause) and also in pregnancy. Plasma cholesterol is associated with different lipoprotein fractions (LDL, VLDL and HDL). Elevation in plasma HDL cholesterol is beneficial to the body, since it protects the body from atherosclerosis and coronary heart diseases (CHD). On the other hand, increase in LDL cholesterol is harmful to the body as it may lead to various complications, including CHD.

Hypercholesterolemia: Increase in plasma cholesterol (>200 mg/dl) concentration is known as hypercholesterolemia and is observed in many disorders.

1. Diabetes mellitus
2. Hypothyroidism (myxedema)
3. Obstructive jaundice
4. Nephrotic syndrome

Control of Hypercholesterolemia

1. Consumption of polyunsaturated fatty acids (PUFA).
2. **Dietary cholesterol:** Cholesterol is found only in animal foods and not in plant foods.
3. **Plant sterols:** Certain plant sterols and their esters reduce plasma cholesterol levels.
4. **Dietary fiber:** Fiber present in vegetables decreases the cholesterol absorption from the intestine.
5. Avoiding high carbohydrate diet.
6. **Impact of lifestyles:** Elevation in plasma cholesterol is observed in people with smoking, abdominal obesity, lack of exercise, stress, high blood pressure, consumption of soft water, etc.
7. **Moderate alcohol consumption:** The beneficial effects of moderate alcohol intake are masked by the ill effects of chronic alcoholism.
8. **Use of drugs:** Drugs such as lovastatin which inhibit HMG CoA reductase and decrease cholesterol synthesis are used. Certain drugs—cholestyramine and colestipol—bind with bile acids and decrease their intestinal reabsorption. Clofibrate increases the activity of lipoprotein lipase and reduces the plasma cholesterol and triacylglycerols.

Hypocholesterolemia: A decrease in the plasma cholesterol is observed in hyperthyroidism, pernicious anemia, malabsorption syndrome, hemolytic jaundice, etc.

Q. 18. Write a note on glycogen storage diseases.

Ans. The metabolic defects concerned with the glycogen synthesis and degradation are collectively referred to as glycogen storage diseases. The inherited disorders are characterized by deposition of normal or abnormal type of glycogen in one or more tissues (see table below).

Q. 19. Write a note on lipid storage disease.

Ans. Glycolipids are derivatives of ceramide (sphingosine bound to fatty acid), hence, they are more appropriately known as **glycosphingolipids**. The simplest form of glycosphingolipids are cerebroside containing ceramide bound to monosaccharides. Galactocerebroside and glucocerebroside are the common glycosphingolipids. Galactocerebroside is a major component of membrane lipids in the nervous

tissue. Glucocerebroside is an intermediate in the synthesis and degradation of complex glycosphingolipids.

Lipid Storage Disease (Sphingolipidoses)

1. **Gaucher's disease:** This is due to a defect in the enzyme β -glucosidase. As a result, tissue glucocerebroside levels increase. This disorder is commonly associated with enlargement of liver and spleen, osteoporosis, pigmentation of skin, anemia, mental retardation, etc.
2. **Krabbe's disease:** Defect in the enzyme β -galactosidase results in the accumulation of galactocerebroside. A total absence of myelin in the nervous tissue is a common feature. Severe mental retardation, convulsions, blindness, deafness, etc. are seen. Krabbe's disease is fatal in early life.
3. **Niemann-Pick disease:** It is an inherited disorder due to a defect in the enzyme sphingomyelinase. This causes accumulation of sphingomyelins in liver and

Type	Name	Enzyme defect	Organ involved	Characteristics
I	von Gierke's disease	Glucose-6-phosphatase	Liver, kidney, intestine	Glycogen accumulates in hepatocytes and renal cells, enlarged liver and kidney, fasting hypoglycemia, lactic acidemia; hyperlipidemia; ketosis, gouty arthritis.
II	Pompe's disease	Lysosomal α -1,4-glucosidase	All organs	Glycogen accumulates in lysosomes in almost all tissues, heart is mostly involved, enlarged liver and heart, nervous system is also affected, death occurs at an early age due to heart failure.
III	Cori's disease (Forbe's disease)	Amylo- α -1,6-glucosidase	Liver, muscle, heart, leukocyte	Branched chain glycogen accumulates in enlarged liver and kidney, fasting hypoglycemia, lactic acidemia; hyperlipidemia; ketosis, gouty arthritis (mild form).
IV	Anderson's disease	Glucosyl 4-6 transferase	Most tissue	A rare disease, glycogen with only few branches accumulate in cirrhosis of liver, impaired liver function.
V	McArdle's disease	Muscle glycogen phosphorylase	Skeletal muscle	Muscle glycogen stores very high, not available during exercise, patient cannot perform strenuous exercise, muscle cramps, blood lactate and pyruvate do not increase after exercise, muscle may get damage due to inadequate energy supply.
VI	Her's disease	Liver glycogen phosphorylase	Liver	Enlarged liver, liver glycogen cannot form glucose, mild hypoglycemia and ketosis.
VII	Tarui's disease	Phosphofructokinase	Skeletal muscle, erythrocytes	Muscle cramps due to exercise, blood lactate not elevated, hemolysis occurs.

spleen, resulting in the enlargement of these organs. Victims of Niemann-Pick disease suffer from severe mental retardation, and death may occur in early childhood.

4. **Farber's disease:** A defect in the enzyme ceramidase results in Farber's disease. This disorder is characterized by skeletal deformation, subcutaneous nodules, dermatitis and mental retardation. It is fatal in early life.
5. **Krabbe's disease:** It is caused by defect in enzyme β -galactosidase. Leading to storage of galactocerebro-sides. There is absence of myelin formation, enlargement of spleen and liver with mental retardation.
6. **Tay-Sachs disease:** This is caused by defective enzyme hexosaminidase A, leading to deposition of gangliosides GM₂. This is characterized by blindness, mental retardation, death within 2–3 years.
7. **Fabry's disease:** It is caused by defect in enzyme β -galactosidase, leading to deposition of ceramide trihexoside. This causes renal failure, skin rash, pain in lower extremities.

Gangliosides are complex glycosphingolipids mostly found in ganglion cells. They contain one or more molecules of N-acetylneuraminic acid (NANA) bound ceramide oligosaccharides. Defect in the degradation of gangliosides causes gangliosidosis, Tay-Sachs disease, etc.

2. ENZYMES, VITAMINS AND MINERALS

Q. 1. Write a short note on competitive inhibition.

(TNMGR, April 1998)

Ans. It is type of reversible inhibition. In this, the inhibitor (I) which closely resembles the real substrate (S) is regarded as a substrate analogue. The inhibitor competes with substrate and binds at the active site of the enzyme but does not undergo any catalysis. As long as the competitive inhibitor holds the active site, the enzyme is not available for the substrate to bind. During the reaction, enzyme-substrate (ES) and enzyme-inhibitor (EI) complexes are formed. The relative concentration of the substrate and inhibitor and their respective affinity with the enzyme determines the degree of competitive inhibition. The inhibition could be overcome by a high substrate concentration. The enzyme succinate dehydrogenase (SDH) is a classical example of competitive inhibition with succinic acid as its substrate. The compounds, namely malonic acid, glutaric acid and oxalic acid, have structural similarity with succinic acid and compete with the substrate for binding at the active site of SDH. Methanol is toxic to the body when it is converted to formaldehyde by the

enzyme alcohol dehydrogenase (ADH). Ethanol can compete with methanol for ADH. Thus, ethanol can be used in the treatment of methanol poisoning.

Antimetabolites: These are the chemical compounds that block the metabolic reactions by their inhibitory action on enzymes. Antimetabolites are usually structural analogues of substrates and thus are competitive inhibitors. They are in use for cancer therapy, gout, etc.

Q. 2. Write a note on factors influencing enzymatic reactions.

(TNMGR, Nov. 1995, April 2007)

Ans.

1. **Concentration of enzyme:** As the concentration of the enzyme is increased, the velocity of the reaction increases.
2. **Concentration of substrate:** Increase in the substrate concentration gradually increases the velocity of enzyme reaction within the limited range of substrate levels.
3. **Effect of temperature:** Velocity of an enzyme reaction increases with increase in temperature up to a maximum and then declines. A bell-shaped curve is usually observed.
4. **Effect of pH:** Each enzyme has an optimum pH at which the velocity is maximum. Below and above this pH, the enzyme activity is much lower and at extreme pH, the enzyme becomes totally inactive.
5. **Effect of product concentration:** The accumulation of reaction products generally decreases the enzyme velocity.
6. **Effect of activators:** Some of the enzymes require certain inorganic metal ions. Two categories of enzymes requiring metals for their activity are distinguished.
 - a. **Metal-activated enzymes:** The metal is not tightly held by the enzyme and can be exchanged easily with other ions, e.g. ATPase (Mg^{2+} and Ca^{2+}).
 - b. **Metalloenzymes:** These enzymes hold the metals rather tightly which are not readily exchanged. e.g. alcohol dehydrogenase, carbonic anhydrase, alkaline phosphatase contain zinc.
7. **Effect of time:** Under ideal and optimal conditions (like pH, temperature, etc.), the time required for an enzyme reaction is less. Variations in the time of the reaction are generally related to the alterations in pH and temperature.
8. **Effect of light and radiation:** Exposure of enzymes to ultraviolet, beta, gamma and X-rays inactivates certain enzymes due to the formation of peroxides. For example, UV rays inhibit salivary amylase activity.

Q. 3. Write a short note on ptyalin. (TNMGR, April 1995)

Ans. Carbohydrates are the only nutrients for which the digestion begins in the mouth to a significant extent. During the process of mastication, salivary α -amylase (ptyalin) acts on starch randomly and cleaves α -1,4-glycosidic bonds. The products formed include α -limit dextrins (containing about 8 glucose units with one or more α -1,6-glycosidic bonds), maltotriose and maltose. Optimum pH necessary for the activation of salivary amylase is 6. Salivary amylase cannot act on cellulose.

Q. 4. Write a note on clinical importance of isoenzymes. (TNMGR, March 2011)

Ans.

1. **Clinical importance of isoenzymes of lactic dehydrogenase (LDH):** Isoenzymes of LDH have immense value in the diagnosis of heart and liver related disorders. In healthy individuals, the activity of LDH₂ is higher than that of LDH₁ in serum. In the case of myocardial infarction, LDH₁ is much greater than LDH₂ and this happens within 12 to 24 hours after infarction. Increased activity of LDH₅ in serum is an indicator of liver diseases. LDH activity in the RBC is 80–100 times more than that in the serum. Hence, for estimation of LDH or its isoenzymes, serum should be totally free from hemolysis or else false positive results will be obtained.
2. **Clinical importance of isoenzymes of creatine phosphokinase (CPK):** In healthy individuals, the isoenzymes CPK₂ (MB) is almost undetectable in serum with less than 2% of total CPK. After the myocardial infarction (MI), within the first 6–18 hours, CPK₂ increases in the serum to as high as 20%. CPK₂ isoenzyme is not elevated in skeletal muscle disorders. Therefore, estimation of the enzyme CPK₂ (MB) is the earliest reliable indication of myocardial infarction.
3. **Clinical importance of isoenzymes of alkaline phosphatase (ALP):** Increase in α_2 -heat labile ALP suggests hepatitis whereas pre β -ALP indicates bone disease.

Q. 5. Write a short note on lactic acid dehydrogenase. (TNMGR, Oct. 2003)

Ans. Lactic acid dehydrogenase (LDH) converts lactic acid into pyruvic acid. It has five distinct isoenzymes; LDH₁, LDH₂, LDH₃, LDH₄, LDH₅. They can be separated by electrophoresis (cellulose or starch gel or agarose gel). LDH₁ has more positive charge and fastest in electrophoretic mobility while LDH₅ is the slowest.

Structure: LDH is an oligomeric (tetrameric) enzyme made up of four polypeptide subunits. Two types of

subunits, namely M (for muscle) and H (for heart) are produced by different genes. M-subunit is basic while H subunit is acidic. The isoenzymes contain either one or both the subunits giving LDH₁ to LDH₅.

- i. LDH₁: 25% of normal serum in humans. Its subunit constitution is H₄. Principal tissue of origin is heart and RBC. It has fastest electrophoretic mobility. It is not destroyed by heat.
- ii. LDH₂: 35% of normal serum in humans. Its subunit constitution is H₃M. Principal tissue of origin is heart and RBC. It has faster electrophoretic mobility. It is not destroyed by heat.
- iii. LDH₃: 27% of normal serum in humans. Its subunit constitution is H₂M₂. Principal tissue of origin is brain and kidney. It has fast electrophoretic mobility. It is partially destroyed by heat.
- iv. LDH₄: 8% of normal serum in humans. Its subunit constitution is HM₃. Principal tissue of origin is liver and skeletal muscle. It has slow electrophoretic mobility. It is destroyed by heat.
- v. LDH₅: 5% of normal serum in humans. Its subunit constitution is M₄. Principal tissue of origin is skeletal muscle and liver. It has slowest electrophoretic mobility. It is destroyed by heat.

Diagnostic importance: In healthy individuals, the activity of LDH₂ is higher than that of LDH₁ in serum. In the case of myocardial infarction, LDH₁ is much greater than LDH₂ and this happens within 12 to 24 hours after infarction. Increased activity of LDH₅ in serum is an indicator of liver diseases.

Q. 6. Write a short note on chemical messenger.

(TNMGR, March 2007)

Ans. The endocrine system acts through a wide range of chemical messengers known as **hormones**. Hormones are conventionally defined as organic substances, produced in small amounts by specific tissues (endocrine glands), secreted into the blood stream to control the metabolic and biological activities in the target cells.

Classification**A. Based on the Chemical Structure**

1. **Protein or peptide hormone:** Insulin, glucagon, antidiuretic hormone, and oxytocin.
2. **Steroid hormone:** Glucocorticoids and mineralocorticoids.
3. **Amino acid derivatives:** Epinephrine, norepinephrine, and thyroxine.

B. Based on the Mechanism of Action

1. **Group I hormones:** These hormones bind to intracellular receptors to form receptor hormone complexes, which binds to DNA. For example, estrogen and calcitriol.
2. **Group II hormones:** These hormones are considered as first messengers, as they bind to cell surface receptors and stimulates the release of certain molecules, second messengers, which perform the biochemical function.
 - i. The second messenger is cAMP. For example, ACTH, FSH, glucagon, and calcitonin.
 - ii. The second messenger is phosphatidyl inositol/calcium. For example, TRH and gastrin.
 - iii. The second messenger is unknown. For example, growth hormone and oxytocin.

Q. 7. Write a note on vitamins and oral cavity.

(Nagpur Uni., Oct. 2004; TNMGR, March 2008)

Ans. Vitamins may be regarded as organic compounds required in the diet in small amounts to perform specific biological functions for normal maintenance of optimum growth and health of the organism

Water-soluble Vitamins

Vitamin B Complex

1. **Thiamine (vitamin B₁ or anti-beriberi or anti-neuritic vitamin):** It has a specific coenzyme/thiamine pyrophosphate (TPP) which is mostly associated with carbohydrate metabolism.

Biochemical functions

- i. The coenzyme, thiamine pyrophosphate (TPP) participate in conversion of pyruvate to acetyl CoA during carbohydrate metabolism.
- ii. TPP also participate in Krebs cycle.
- iii. Transketolase, enzyme required during hexose monophosphate shunt, is dependent on TPP.
- iv. TPP plays an important role in transmission of nerve impulse by acetylcholine synthesis.

Recommended dietary allowance (RDA): 1–1.5 mg/day for adults. 0.7–1.2 mg/day for children. 2 mg/day for pregnant, lactating, old age and alcoholics.

Dietary source: Cereals, pulses, oil seeds, nuts, yeast, animal foods like pork, liver, heart, kidney, milk, etc.

Deficiency symptoms

- a. The deficiency of vitamin B₁ results in a condition called **beriberi**. The early symptoms of thiamine deficiency are loss of appetite (anorexia), weakness, constipation, nausea, mental depression, peripheral neuropathy, irritability, etc.

- i. **Wet beriberi:** Edema of legs, face, trunk and serous cavities, breathlessness and palpitation. The systolic blood pressure is elevated while diastolic is decreased with fast and bouncing pulse is observed. The heart becomes weak and death may occur due to heart failure.
- ii. **Dry beriberi:** This is associated with neurological manifestations resulting in peripheral neuritis. The muscles become progressively weak and walking becomes difficult. The affected individuals depend on support to walk and become bedridden, and may even die if not treated.
- b. **Wernicke-Korsakoff syndrome:** Mostly seen in chronic alcoholics, as the body demands of thiamine increase in alcoholism. It is characterized by loss of memory, apathy and rhythmical to and fro motion of the eyeballs.

2. **Riboflavin (vitamin B₂):** Riboflavin through its coenzymes takes part in a variety of cellular oxidation-reduction reactions.

Coenzymes of riboflavin: Flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD).

Biochemical functions

- i. The flavin coenzymes participate in many redox reactions responsible for energy production.
- ii. The coenzymes are associated with certain enzymes involved in carbohydrate, lipid, protein and purine metabolisms, besides the electron transport chain.

RDA: For adults—1.2–1.7 mg/day.

Dietary sources: Milk and milk products, meat, eggs, liver, kidney are rich sources. Cereals, fruits, vegetables and fish are moderate sources.

Deficiency symptoms: Riboflavin deficiency symptoms include cheilosis (fissures at the corners of the mouth), glossitis (tongue smooth and purplish) and dermatitis.

3. **Niacin:** Niacin or nicotinic acid is also known as pellagra preventive (PP) factor of Goldberg. The coenzymes of niacin (nicotinamide adenine dinucleotide—NAD⁺ and nicotinamide adenine dinucleotide phosphate—NADP⁺) can be synthesized by the essential amino acid and tryptophan.

Biochemical functions

- i. The coenzymes NAD⁺ and NADP⁺ are involved in a variety of oxidation-reduction reactions.
- ii. A large number of enzymes belonging to the class oxidoreductases are dependent on NAD⁺ or NADP⁺.
- iii. NADH produced is oxidized in the electron transport chain of generate ATP.

- iv. NADPH is also important for many biosynthetic reactions as it donates reducing equivalents.

RDA: For adults—15–20 mg for children—10–15 mg.

Dietary sources: Liver, yeast, whole grains, cereals, pulses, milk, fish, eggs, and vegetables.

Deficiency symptoms: Niacin deficiency results in a condition called **pellagra** (Italian: *Rough skin*). This disease involves skin, gastrointestinal tract and central nervous system. The symptoms of pellagra are commonly referred to as **three Ds**.

Dermatitis (inflammation of skin) is usually found in the areas of the skin exposed to sunlight (neck, dorsal part of feet, ankle and parts of face).

Diarrhea may be in the form of loose stools, often with blood and mucus. Prolonged diarrhea leads to weight loss.

Dementia is associated with degeneration of nervous tissue. The symptoms of dementia include anxiety, irritability, poor memory, insomnia (sleeplessness).

4. **Pyridoxine (vitamin B₆):** Vitamin B₆ is used to collectively represent the three compounds, namely pyridoxine, pyridoxal and pyridoxamine (the vitamers of B₆). The active form of vitamin B₆ is the coenzyme pyridoxal phosphate (PLP).

Biochemical functions

- Pyridoxal phosphate (PLP) is closely associated with the metabolism of amino acids.
- The synthesis of certain specialized products such as serotonin, histamine, niacin coenzymes from the amino acids is dependent on pyridoxine.
- Pyridoxal phosphate participates in reactions like transamination, decarboxylation, deamination, transsulfuration, condensation, etc.
- Pyridoxal phosphate is required for the synthesis of δ -aminolevulinic acid, the precursor for heme synthesis.
- PLP is needed for the absorption of amino acids from the intestine.
- Adequate intake of B₆ is useful to prevent urinary stone formation.

RDA: For adults—2–2.2 mg/day.

Dietary sources: Animal sources such as egg yolk, fish, milk, meat; vegetable sources include wheat, corn, and cabbage.

Deficiency symptoms: Neurological symptoms such as depression, irritability, nervousness, mental confusion, convulsions, and peripheral neuropathy, decreased hemoglobin concentration.

5. **Biotin:** Biotin (formerly known as anti-egg white injury factor, vitamin B₇ or vitamin H) is a sulfur containing B-complex vitamin. It directly participates as a coenzyme in the carboxylation reactions.

Biochemical functions

- Biotin serves as carrier of CO₂ in carboxylation reactions.
- As coenzyme, it is involved in gluconeogenesis and fatty acid synthesis.
- Metabolism is dependent on propionyl CoA and leucine.

RDA: For adults: 100–300 mg.

Dietary sources: Liver, kidney, egg yolk, milk, tomatoes, grains, etc.

Deficiency symptoms: anemia, loss of appetite, nausea, dermatitis, glossitis, depression, hallucinations, muscle pain and dermatitis.

6. **Pantothenic acid:** Pantothenic acid, formerly known as chick anti-dermatitis factor (or filtrate factor) is widely distributed in nature. Its metabolic role as coenzyme A is also widespread.

Biochemical functions

- Coenzyme A is a central molecule involved in the metabolism of carbohydrate, lipid and proteins.
- It plays unique role in integrating various metabolic pathways.

Pantothenic acid is involved in formation of fatty acids.

RDA: For adults: 5–10 mg.

Dietary sources: Eggs, liver meat, yeast, milk, etc.

Deficiency symptoms: Burning feet syndrome (pain and numbness in the toes, sleeplessness, fatigue).

7. **Folic acid:** Folic acid or folacin is abundantly found in green leafy vegetables. It is important for one carbon metabolism and is required for the synthesis of certain amino acids, purines and the pyrimidine-thymine.

Biochemical functions

- Tetrahydrofolate (THF or FH₄), the coenzyme of folic acid is actively involved in one carbon metabolism, amino acid and nucleotide metabolism.
- One carbon metabolism synthesizes purines, pyrimidine, and glycine.

RDA: For adults: 200 µg/day.

Dietary sources: Green leafy vegetables, whole grains, cereals, liver, kidneys, yeast, and eggs.

Deficiency symptoms: Megaloblastic anemia and neural defects in fetus.

8. **Cobalamin (vitamin B₁₂):** Vitamin B₁₂ is also known as anti-pernicious anemia vitamin. It is a unique vitamin, synthesized by only microorganisms and not by animals and plants. The vitamin B₁₂ is present in the diet in a bound form to proteins. B₁₂ is liberated by the enzymes, acid hydrolases, in the stomach. The

dietary source of B_{12} is known as extrinsic factor of Castle. The stomach secretes a special protein called intrinsic factor (IF). The cobalamin-IF complex travels through the gut. The complex binds to specific receptors on the surface of the mucosal cells of the ileum. In the mucosal cells, B_{12} is converted to methylcobalamin. It is then transported in the circulation in a bound form to proteins, namely transcobalamins.

Biochemical functions

- i. It participates in the synthesis of methionine from homocysteine.
- ii. It participates in isomerization of methylmalonyl CoA to succinyl CoA.

RDA: For adults: 3 μg /day. For children: 0.5–1.5 μg /day.

Dietary sources: Foods of animal origin.

Deficiency symptoms: Pernicious anemia (low hemoglobin, reduced RBCs, neurological manifestations—neuronal degeneration and demyelination of nervous system—paresthesia (numbness and tingling) of fingers and toes, confusion, loss of memory, and psychosis).

Q. 8. Write a short note on ascorbic acid.

(TNMGR, April 1995)

Ans. Vitamin C is a water-soluble vitamin. It plays an important role in human health and disease.

Chemistry: Ascorbic acid is a hexose derivative and closely resembles monosaccharides in structure. The acidic property of vitamin C is due to the enolic hydroxyl groups. It is a strong reducing agent.

Biosynthesis and metabolism: Many animals can synthesize ascorbic acid from glucose via uronic acid pathway. However, many other primates, guinea pigs and bats cannot synthesize ascorbic acid due to the deficiency of enzyme L-gluconolactone oxidase. Vitamin C is rapidly absorbed from the intestine, it is not stored in the body to a significant extent. Ascorbic acid is excreted in urine as such, or as its metabolites diketogluconic acid and oxalic acid.

Biochemical functions

1. **Collagen formation:** Vitamin C plays the role of a coenzyme in hydroxylation of proline and lysine while procollagen is converted to collagen.
2. **Bone formation:** Bone tissues possess an organic matrix, collagen and the inorganic calcium, phosphate, etc.
3. **Iron and hemoglobin metabolism:** Ascorbic acid enhances iron absorption by keeping it in the ferrous

form. Vitamin C is useful in the reconversion of methemoglobin to hemoglobin. The degradation of hemoglobin to bile pigments requires ascorbic acid.

4. **Tryptophan metabolism:** Vitamin C is essential for the hydroxylation of tryptophan (enzyme-hydroxylase) to hydroxytryptophan in the synthesis of serotonin.
5. **Tyrosine metabolism:** Ascorbic acid is required for the oxidation of p-hydroxyphenylpyruvate (enzyme hydroxylase) to homogentisic acid in tyrosine metabolism.
6. **Folic acid metabolism:** The active form of the vitamin folic acid is tetrahydrofolate (FH_4). Vitamin C is needed for the formation of FH_4 (enzyme-folic acid reductase). Further, in association with FH_4 , ascorbic acid is involved in the maturation of erythrocytes.
7. **Peptide hormone synthesis:** Many peptide hormones contain carboxyl terminal amide which is derived from terminal glycine. Hydroxylation of glycine is carried out by peptidylglycine hydroxylase which requires vitamin C.
8. **Synthesis of corticosteroid hormones:** Adrenal gland possesses high levels of ascorbic acid, particularly in periods of stress.
9. **Sparing action of other vitamins:** Ascorbic acid is a strong antioxidant. It spares vitamin A, vitamin E, and some B-complex vitamins from oxidation.
10. **Immunological function:** Vitamin C enhances the synthesis of immunoglobulins (antibodies) and increases the phagocytic action of leukocytes.
11. **Preventive action on cataract:** Vitamin C reduces the risk of cataract formation.
12. **Preventive action on chronic diseases:** As an antioxidant, vitamin C reduces the risk of cancer, cataract, and coronary heart diseases.

Recommended dietary allowance (RDA): About 60–70 mg vitamin C intake per day will meet the adult requirement. Additional intake (20–40%) is recommended for women during pregnancy and lactation.

Dietary sources: Citrus fruits, gooseberry (amla), guava/green vegetables (cabbage, spinach), tomatoes, potatoes (particularly skin) are rich in ascorbic acid.

The deficiency of ascorbic acid results in scurvy. This disease is characterized by spongy and sore gums, loose teeth, anemia, swollen joints, fragile blood vessels, decreased immunocompetence, delayed wound healing, sluggish hormonal function of adrenal cortex and gonads, hemorrhage, osteoporosis, etc. Most of these symptoms are related to impairment in the synthesis of collagen and/or the antioxidant property of vitamin C.

Q. 9. Write short notes on fat-soluble vitamins.*(TNMGR, April 2014)***Q. Write short notes on sources, requirements and functions of vitamin A.***(TNMGR, March 2009)***Q. Write short notes on cholecalciferol.***(TNMGR, Oct. 1999)***Ans.**

1. **Vitamin A:** The fat soluble vitamin A, as such is present only in foods of animal origin. However, its provitamins carotenes are found in plants. The term retinoid is often used to include the natural and synthetic forms of vitamin A. Retinol, retinal and retinoic acid are regarded as vitamers of vitamin A.

Dietary retinyl esters are hydrolyzed by pancreatic or intestinal brush border hydrolases in the intestine, releasing retinol and free fatty acids. Carotenes are hydrolyzed to retinal which is reduced to retinol. In intestinal mucosal cells, retinol is converted to long chain fatty acids, incorporated into chylomicrons and transferred to lymph. The retinol esters of chylomicrons are taken up by liver and stored. Retinol is transported in circulation by plasma retinol binding protein.

Biochemical functions

- i. Vitamin A helps in vision.
- ii. Retinol and retinoic acid regulate the protein synthesis and involved in cell growth and differentiation.
- iii. Vitamin A is essential to maintain healthy epithelial tissue.
- iv. Retinyl phosphate is required for the synthesis of certain glycoproteins required for growth and mucus secretion.
- v. Retinol and retinoic acid are involved in iron transport by synthesizing transferrin.
- vi. Vitamin is needed for proper maintenance of immune system.
- vii. Cholesterol synthesis requires vitamin A.
- viii. Carotenoids function as antioxidants.

RDA: For adults: 1000/800 retinol equivalents (male/female).

Dietary sources: Liver, kidney, egg yolk, milk, cheese, fish, yellow and dark green vegetables.

Deficiency symptoms

- i. Night blindness (nyctalopia)
- ii. **Xerophthalmia:** Dryness of conjunctiva and cornea, keratinization of epithelial cells with white triangular plaques on conjunctiva (**Bitot's spots**)
- iii. **Keratomalacia:** Destruction of cornea.

- iv. Total blindness
- v. Growth retardation
- vi. Sterility in males
- vii. Rough and dry skin
- viii. Increased tendency for stone formation.

2. **Vitamin D:** It resembles sterols in structure and functions like a hormone. Ergocalciferol (vitamin D₂) is formed from ergosterol and is present in plants. Cholecalciferol (vitamin D₃) is found in animals.

Biochemical functions

- i. Calcitriol increases the intestinal absorption of calcium and phosphate.
- ii. Calcitriol stimulates calcium uptake for deposition as calcium phosphate, in bone.
- iii. Calcitriol decreases excretion and increases reabsorption of calcium and phosphate in the kidneys.

RDA: 400 IU.

Dietary sources: Fatty fish, fish liver oils, egg yolk, skin exposure to sunlight, consumption of natural foods.

Deficiency symptoms

- i. **Rickets in children:** Soft and pliable bones, bow-legs, decreased plasma calcitriol, and elevated alkaline phosphatase.
- ii. **Osteomalacia in adults:** Soft bone, and pathological fractures.
- iii. **Renal rickets:** Seen in patients with chronic renal failure, due to decreased synthesis of calcitriol in kidneys.

3. **Vitamin E:** Vitamin E (tocopherol) is a naturally occurring antioxidant. It is also known as **anti-sterility vitamin** and **vitamin in search of a disease**. Vitamin E is absorbed along with fat in the small intestine. Bile salts are necessary for the absorption. In the liver, it is incorporated into lipoproteins (VLDL and LDL) and transported. Vitamin E is stored in adipose tissue, liver and muscle. The normal plasma level of tocopherol is less than 1 mg/dl.

Biochemical functions

- i. It is potent antioxidant, prevents the non-enzymatic oxidations of various cell components by oxygen and free radicals.
- ii. It protects the polyunsaturated fatty acids from peroxidation reactions.
- iii. It is regarded as membrane antioxidant, as it is essential for membrane structure and integrity of the cell.

- iv. It prevents sterility.
- v. It increases the synthesis of heme.
- vi. It is required for cellular respiration.
- vii. It prevents oxidation of vitamin A and carotenes.
- viii. It is required for proper storage of creatine in skeletal muscle.
- ix. It is required for absorption of amino acids from intestine.
- x. It is involved in synthesis of nucleic acids.
- xi. It protects liver from damage caused by toxins.

RDA: 10/8 mg/day for male/female.

Dietary sources: Vegetable oils, meat, milk, butter, eggs.

Deficiency symptoms: Sterility, degenerative changes in muscle, megaloblastic anemia, increased fragility of erythrocytes, neurological symptoms.

4. **Vitamin K:** Vitamin K is the only fat-soluble vitamin with a specific coenzyme function. It is required for the production of blood clotting factors, essential for coagulation. Vitamin K is taken in the diet or synthesized by the intestinal bacteria. Its absorption takes place along with fat (chylomicrons) and is dependent on bile salts. Vitamin K is transported along with LDL and is stored mainly in liver, and to a lesser extent in other tissues.

Biochemical functions

- i. It brings the post-translational modification of blood clotting factors.
- ii. Acts as a coenzyme for the carboxylation of glutamic acid residues present in proteins.
- iii. It is required for carboxylation of glutamic acid residue of osteocalcin.

RDA: 70–140 µg/day.

Dietary sources: Cabbage, cauliflower, tomatoes, alfalfa, spinach, other green vegetables, egg yolk, meat, liver, and cheese.

Deficiency symptoms: Lack of active prothrombin leading to altered blood coagulation.

Q. 10. Write about role of trace elements.

(TNMGR, April 2012; BPUHS, Nov. 2012; PAHER, April 2013)

Ans. The trace elements (microminerals) are required in amounts less than 100 mg/day. Their role are as follows:

- 1. **Iron:** Constituents of heme, e.g. hemoglobin, myoglobin; involved in transport and biological oxidation.
- 2. **Copper:** Constituent of enzymes, e.g. cytochrome c oxidase, catalase; in iron transport.

- 3. **Iodine:** Constituent of thyroxine and triiodothyronine.
- 4. **Manganese:** Cofactor for enzymes, e.g. arginase; glycoprotein synthesis.
- 5. **Zinc:** Cofactor for enzymes, e.g. alcohol dehydrogenase, carbonic anhydrase.
- 6. **Molybdenum:** Constituent of enzymes, e.g. xanthine oxidase.
- 7. **Cobalt:** Constituent of vitamin B₁₂ required for the formation of erythrocytes.
- 8. **Fluorine:** Helps in proper formation of bone and teeth.
- 9. **Selenium:** Involved in antioxidant function along with vitamin E; constituent of glutathione peroxidase and selenocysteine.
- 10. **Chromium:** Promotes insulin function.

Q. 11. Write about deficiency and toxicity symptoms of fluoride.

(TNMGR, April 2015)

Q. Write short notes on fluorosis. (TNMGR, Sept. 2002)

Q. Write about role of fluorides in dental health.

(TNMGR, Sept. 2008)

Ans. Fluoride is mostly found in bones and teeth. The beneficial effects of fluoride in trace amounts are overshadowed by its harmful effects caused by excess consumption.

Biochemical Functions

- 1. Fluoride prevents the development of dental caries. It forms a protective layer of acid resistant fluorapatite with hydroxyapatite of the enamel and prevents the tooth decay by bacterial acids. Further, fluoride inhibits the bacterial enzymes and reduces the production of acids.
- 2. Fluoride is necessary for the proper development of bones.
- 3. It inhibits the activities of certain enzymes. Sodium fluoride inhibits enolase (of glycolysis) while fluoroacetate inhibits aconitase (of citric acid cycle).

Dietary requirement and sources: An intake of less than 2 ppm of fluoride will meet the daily requirements. Drinking water is the main source.

Disease States

- 1. **Dental caries:** It is clearly established that drinking water containing less than 0.5 ppm of fluoride is associated with the development of dental caries in children.
- 2. **Fluorosis:** Excessive intake of fluoride is harmful to the body. An intake above 2 ppm (particularly >5 ppm) in children causes mottling of enamel and

discoloration of teeth. The teeth are weak and become rough with characteristic brown or yellow patches on their surface. These manifestations are collectively referred to as dental fluorosis. An intake of fluoride above 20 ppm is toxic and causes pathological changes in the bones. Hypercalcification increasing the density of the bones of limbs, pelvis and spine, is a characteristic feature. Even the ligaments of spine and collagen of bones get calcified. Neurological disturbances are also commonly observed. The manifestation described here constitute skeletal fluorosis. In the advanced stages, the individuals are crippled and cannot perform their daily routine work due to stiff joints. This condition of advanced fluorosis is referred to as **genu valgum**.

3. DIET AND NUTRITION

Q. 1. Define diet and nutrition. Discuss the importance of diet in dentistry.

(BFUHS, May 2007; UHSR, April 2009)

Q. Discuss role of nutrition in prevention of dental diseases.

(TNMGR, March 2007)

Ans. Diet is defined as the types and amounts of food eaten daily by an individual.

Nutrition is defined as the sum of the processes by which an individual takes in and utilizes food.

Malnutrition is a pathological state resulting from a relative or absolute deficiency or excess of one or more essential nutrients.

Classification of Foods

a. *By origin*

- Animal origin
- Vegetable origin

b. **By chemical composition:** Proteins, fats, carbohydrates, vitamins, and minerals.

c. *By predominant function*

- *Body building foods*—milk, meat, and poultry.
- *Energy giving foods*—cereals, sugars, and roots.
- *Protective foods*—vegetables, fruits, and milk.

d. **By nutritive value:** Cereals and millets, pulses, vegetables, nuts and oilseeds, fruits, animal foods, fats and oils, sugar and jaggery.

Nutrients: These are organic and inorganic complexes contained in food. Each nutrient has specific functions in the body. They are divided into:

a. *Macronutrients:*

- Proteins—7–15%
- Fats—10–30%
- Carbohydrates—65–80%

b. *Micronutrients*

- Vitamins
- Minerals

Proteins: They are complex inorganic nitrogenous compounds composed of carbon, hydrogen, oxygen, nitrogen and sulfur. Their major functions are:

1. Body building.
2. Repair and maintenance of tissues.
3. Synthesis of antibodies, plasma proteins, haemoglobin, enzymes and hormones.
4. The supply energy (4 kcal/g).

Proteins are obtained from animal sources (milk, meat, egg) and from vegetable sources (pulses, cereals, nuts). The Indian council of medical research has recommended one gram protein/kg body weight for adult.

Fats/lipids: They are classified as

- *Simple lipids*—triglycerides.
- *Compound lipids*—phospholipids.
- *Derived lipids*—cholesterol.

Functions

1. They supply energy (9 kcal/g)
2. They carry flavour of food.
3. They add satiety and variety to a meal.
4. They are an integral part of cells and cell membranes.
5. They carry the fat-soluble vitamins.
6. They may act to reduce dental caries by coating the plaque, thereby preventing fermentable carbohydrates from entering it.

Fats are obtained from animal sources (ghee, butter, cheese, egg, fat of meat and fish), vegetable sources (groundnut, coconut, mustard) and other sources (rice, wheat, jowar). The Indian council of medical research has recommended a daily intake of not more than 20% of total energy intake through fats.

Carbohydrates: They are found in cereals, fruits and vegetables and are essential in the diet as a source of both glucose and cellulose, the major source of energy. Their major functions are:

1. They supply energy (4 kcal/g).
2. They are essential for the oxidation of fats.
3. They are required for the synthesis of certain non-essential amino acids.

The 3 main sources of carbohydrates are starches, sugars and cellulose.

Vitamins: These are substances which must be obtained by dietary means because of a lack of capacity in the human body to synthesize it. They are part of the enzyme system (act either as coenzymes/catalysts for

energy-releasing reactions from carbohydrates, lipids and proteins).

Classification of Vitamins

- **Fat-soluble:** A, D, E, K
- **Water-soluble:** B, C

Minerals

Classification of Minerals

- **Major minerals:** Calcium, phosphorus, sodium, potassium, and magnesium.
- **Trace elements:** Iron, iodine, fluorine, zinc, copper, cobalt, chromium, manganese, molybdenum, selenium, nickel, tin, silicon, and vanadium.
- **Trace contaminants with no known function:** Lead, mercury, barium, boron, and aluminum.

Calcium: The best natural sources are milk, and milk products, eggs and fish. Its functions are:

1. Formation of bones and teeth
2. Coagulation of blood
3. Contraction of muscles
4. Milk production
5. Keeping the cell membranes intact
6. Metabolism of enzymes and hormones

A daily intake of 400 to 500 mg is required for adults.

Phosphorus: It is widely distributed in food stuffs. It is essential for the formation of bones and teeth. Although, specific requirements have not been recommended, some researchers have suggested that its intake should be at least equal to that of calcium.

Iron: It is found in meat, liver, fish, cereals, green leafy vegetables, nuts and dried fruits. It is required for

1. Formation of hemoglobin
2. Brain development and function
3. Muscle activity

A daily intake of 0.9 mg and 2.8 mg is required for adult males and females respectively. Deficiency is characterized by:

- Iron deficiency anemia
- Impaired cell-mediated immunity
- Reduced resistance to infection
- Diminished work performance

Iodine: The best sources are sea foods and cod liver oil. It is required for:

1. Synthesis of thyroid hormone
2. Normal growth and development

A daily intake of 150 µg is required for adults.

The most obvious deficiency is goiter. The other features are:

- Hypothyroidism
- Retarded physical and mental development
- Dwarfism

Nutrition and malocclusion: Teeth differentiate early in development and undergo short critical periods of growth. Therefore, the ultimate genetically determined size is established early in the developmental process. In contrast, jaw bones develop during an extended period of time, undergo a prolonged critical period and achieve their genetic size potential only after the teeth have developed. Because tooth sizes are determined genetically in a much shorter time span whereas jaw size determination takes longer, a chronic postnatal malnutrition would result in stunted jaw development after the teeth have differentiated. This may result in class I type of malocclusions. Poor tooth alignment and crowding result in increased caries and periodontal disease.

Nutrition and periodontal disease: Periodontal diseases may involve episodic, progressive disruption of several different tissues. The different host factors are susceptible to nutritional influences acting systemically on structure, repair and defence. The main targets in nutritional deficiency are the epithelial barrier and attachment, periodontal ligament, gingival connective tissue, alveolar bone, cellular and humoral immune mechanisms, inflammatory response, composition of gingival fluid as also the crevicular epithelium (to invasion by antigenic or enzymatic irritants/toxins produced by bacteria). All these are susceptible to nutrient imbalance.

Nutrition and oral cancer: Nutrition plays an important role in the etiology of oral and pharyngeal cancers. Malnutrition increases the susceptibility to cancer of head and neck. Foods contain both initiators and modifiers of carcinogenesis. The modifiers may affect carcinogenesis by influencing the activity of carcinogen-metabolizing enzymes, hormonal status, or the immune response.

Most chemical carcinogens require enzymatic activation. The primary enzyme system responsible is the mixed-function oxidase system which is significantly influenced by the nutritional status and the levels of specific nutrients, e.g. by protein or fat intake. Specific nutrient deficiencies may depress these enzymes, thereby reducing the body's defence against chemical carcinogens.

High-protein diets are likely to contain large amounts of animal and other saturated fats and calories (both associated with cancer). A minimal protein level of about 5% is necessary for good health and growth. High intakes of saturated animal fats are associated with an increased risk of cancer of mouth and pharynx. Malnutrition or anemia reduces the ability of the immune system to counteract neoplastic cells.

Nutritional factors protect against tumorigenesis by

- Acting as blocking agents.
- Altering metabolism of the carcinogen through decreased activation.
- Increasing detoxification.
- By scavenging the active molecular species of carcinogens to prevent their reaching or reacting with target sites in the cell.
- Competitive inhibition.

Vitamin A and Retinoid (Derivatives of Vitamin A)

- Inhibits chemically—induced tumors in various tissues.
- Consumption is linked to lower risk of various cancers in humans.
- People with highest total carotenoid concentrations are 1/3rd at risk of oral and pharyngeal cancers.
- Less toxic synthetic analogue, the retinoid, are effective in preventing carcinogenesis or in inducing regression of already formed tumors.
- Affects tumor latency by retarding growth of tumors.
- Have effects on protein kinase C, which influences epidermal growth factor receptors and DNA synthesis inhibition.
- Retinoid and analogues used topically and systemically have been successful in the treatment of oral leukoplakia.

β -carotene (Which is Metabolised to Vitamin A)

- It is an antioxidant and free radical scavenger.
- Better than retinoid (lower toxicity).
- Inverse relationship is seen between incidence of oral cancer and dietary availability of β -carotene/retinoid and vitamin C.
- Micronuclei formation in (exfoliated) buccal cells is reversed by β -carotene supplementation.
- Patients with oral leukoplakia treated with all-*trans*-retinoic acid, 13-*cis*-retinoic acid or β -carotene showed reductions in lesion size or stabilization of the leukoplakia.

Vitamin C

- It is an antioxidant.
- Negatively associated with risk of oral cancer.

- Inhibits formation of carcinogenic N-nitroso (nitrosamine) compounds and mutagenicity of certain direct-acting mutagens (β -propiolactone and methylnitrosoguanidine).
- Combined vitamin A and C intake is inversely associated with the risk for oral cancer, vitamin A having a more significant impact than vitamin C.
- Enhancer of immune responses through effects on phagocytes.
- Affecter of oxidases involved in detoxification of carcinogens.

Vitamin E

- Users have half the risk of developing oral cancer compared to non-users.
- An antioxidant.
- A free radical scavenger and protects cell membrane from oxidative damage.
- Blocks nitrosamine formation.
- Influences humoral and cell-mediated immunity.
- Increases cell-repair capacity.

Vitamin B complex: Patients with cancer or pre-cancerous lesions in the mouth display signs of vitamin B complex deficiencies.

Foodstuffs

- Risk of cancer of the mouth and pharynx is halved in those who eat fruits/vegetables daily.
- Fish buttermilk, milk, dairy products, oranges, cabbage and sea food are protective against oral cancer. Frequent consumption of milk, eggs, meat or fish reduces the risk of oral carcinogenesis in smokers and betel-nut chewers.
- Increased oral cancer risk was observed for vegetable oil and excess animal fat.

Supplementation with iron and vitamins markedly reduced the incidence of cancers of mouth, pharynx and esophagus. Deficiency may lead to a premalignant state in the oral mucosa (oral mucosal atrophy in iron deficiency states is a predisposing factor in the development of oral cancer).

Q. 2. Discuss the role of nutrition in prevention of dental caries. (BFUHS, May 2008)

Ans. Pre-eruptive effects: Malnutrition can cause irreversible changes in the teeth that could predispose them to develop caries. Enamel malnutrition, physical and chemical composition, time of eruption, tooth morphology and size are all affected by pre-eruptive nutrient intake. Mineral malnutrition may be due to inadequate quantities of calcium and phosphorus,

another mineral showing signs of being an important factor in caries resistance is iron. The dental dysplasia associated with malnutrition:

- An odontoclasia in the deciduous dentition.
- A “yellow teeth” condition seen in permanent teeth.
- “Infantile melanodontia” which has been observed in deciduous teeth.
- A linear hypoplasia of deciduous incisor teeth occurs due to a deficiency in ascorbic acid or vitamin A or neonatal infection.

These hypoplastic defects are caused by interactions between nutrient deficiencies and the processes that occur during tooth development. Enamel hypoplasia is caused specifically by hypocalcemia.

In l-ascorbic acid deficiency, the teeth are qualitatively and quantitatively deficient dentin formation with atrophic calcification or pulpal stone formation. In vitamin D deficiency, hypoplastic lesions of the enamel usually occur. These defects can lead to extensive dental caries.

Post-eruptive effects: The post-eruptive effects of malnutrition (particularly protein deficiency) lead to decreased salivary lysozyme and secretory IgA levels. Changes in salivary peroxidase, lactoferrin, lysozyme and other protein can reduce the host defence mechanism to cariogenic organisms. In children with protein-calorie malnutrition, IgA is reduced in the secretions, thereby increasing caries susceptibility. However, underfed populations may lack the cariogenic challenge that is necessary for the disease to develop. Therefore, their dental caries prevalence may also be low. It is only upon exposure to carcinogenic conditions that their teeth seem to “melt” or deteriorate.

Q. 3. Write a note on balanced diet.

(KLE Uni. Jan. 2009; TNMGR, March 2010, 2011; RGUHS, Oct. 2010; MUHS, June 2010; HP, May 2015)

Ans. Balanced diet or prudent diet is defined as the diet which contains different types of foods, possessing the nutrients—carbohydrates, fats, proteins, vitamins and minerals, in a proportion to meet the requirements of the body. A balanced diet invariably supplies a little more of each nutrient than the minimum requirement to withstand the short duration of leanness and keep the body in a state of good health.

The basic composition of balanced diet is highly variable, as it differs from country to country, depending on the availability of foods. Social and cultural habits, besides the economic status, age, sex and physical activity of the individual largely influence the intake of diet.

The nutrition expert group, constituted by the Indian council of medical research has recommended the

composition of balanced diets for Indians. This is done taking into account the commonly available foods in India. The Indian balanced diet is composed of cereals (rice, wheat, jowar), pulses, vegetables, roots and tubers, fruits, milk and milk products, fats and oils, sugar and groundnuts. Meat, fish and eggs are present in the non-vegetarian diets. In case of vegetarians, an additional intake of milk and pulses is recommended.

Balanced diet in developed countries: Some people in developed countries consume excessive quantities of certain nutrients. It is recommended that such people have to reduce the intake of total calories, total fat, saturated fatty acids, cholesterol, refined sugars and salt. The US government recommends a daily intake of less than 30% fat against the present 40–50% towards calories.

Food pyramid: The food guide pyramid can help to choose a variety of foods to help achieve a balanced diet. Selecting foods from each group will provide the many nutrients needed by the body.

Recommended dietary allowance (RDA): Recommended dietary allowance is the amount of nutrients sufficient for the maintenance of health in nearly all people.

The amounts recommended include

- A minimal physiological requirement (lack of which would eventually cause deficiency disease).
- A margin of safety of 30–50% above actual physiological requirements to allow for individual variation and to provide body stores for times of stress.

The recommendations by the expert committee are:

- Dietary fat should be 20–30% of total daily intake.
- Saturated fats not more than 10% of total energy intake.
- Excessive consumption of refined carbohydrate to be avoided.
- Energy-rich sources such as fats and alcohols—consumption to be restricted.
- Salt intake reduced to not more than 5 gm/day.
- Protein 15–20% of daily intake.
- Reduced consumption of colas, ketchups, and other foods that supply empty calories.

Q. 4. Write about importance of nutrition in an edentulous patient.

(TNMGR, March 2008; BFUHS, Oct. 2010)

Ans. A major problem of many elderly persons is limited physiological capability to digest and absorb foods due to:

1. An inability to chew food thoroughly because of an inadequate/poorly functioning dentition.
2. Appetite is diminished and appreciation of flavourful tastes is lacking which diminishes the food intake.
3. Dental and medical infirmities that interfere with chewing, digestion, or metabolism contribute to a poor nutritional status.
4. Certain nutritionally related maladies (diabetes, obesity, cardiovascular disease, osteoporosis and cancer) require special dietary regimens that necessitate combined guidance and supervision of a team of specialists in medicine, dentistry, dietetics, sociology and psychology.

Alveolar osteoporosis: Alveolar bone participates in the maintenance of body calcium balance making it susceptible to osteoporosis. In the elderly, there is a relative increase in bone disease and resorption compared with deposition. With the loss of teeth, the alveolar process no longer serves its primary function of tooth support and is resorbed. Therefore, the elderly need to supplement their diet (especially in women) with vitamin D and calcium, adequate polyunsaturated fats and low-cost proteins, fewer calories, increased vitamin C and B₁₂, folic acid, iron and other vitamin B members to increase resistance of bone to mechanical and nutritional biochemical stresses.

Q. 5. Write a note on basal metabolic rate.

(TNMGR, Nov. 1995, April 1998)

Ans. Basal metabolism or basal metabolic rate (BMR) is defined as the minimum amount of energy required by the body to maintain life at complete physical and mental rest in the post-absorptive state (i.e. 12 hours after the last meal). It may be noted that resting metabolic rate (RMR) is in recent use for BMR.

Under the basal conditions, although the body appears to be at total rest, several functions within the body continuously occur. These include working of heart and other organs, conduction of nerve impulse, reabsorption by renal tubules, gastrointestinal motility and ion transport across membranes (Na⁺-K⁺ pump consumes about 50% of basal energy).

Measurement of BMR: Either by apparatus of Benedict and Roth or by the Douglas bag method.

Normal value of BMR: For an adult man 35–38 cal/m²/hr;

For an adult woman 32–35 cal/m²/hr.

A BMR value between –15% and +20% is considered as normal.

Factors Affecting BMR

1. **Surface area:** The BMR is directly proportional to the surface area.
2. **Sex:** Men have higher BMR than women.
3. **Age:** In infants and growing children, BMR is higher. In adults, BMR decreases at the rate of about 2% per decade of life.
4. **Physical activity:** BMR is increased in persons with regular exercise.
5. **Hormones:** BMR is raised in hyperthyroidism and reduced in hypothyroidism. The other hormones such as epinephrine, cortisol, growth hormone and sex hormones increase BMR.
6. **Environment:** In cold climates, the BMR is higher compared to warm climates.
7. **Starvation:** During the periods of starvation, BMR decreases up to 50%.
8. **Fever:** Fever causes an increase in BMR.
9. **Disease states:** BMR is elevated in various infections, leukemias, polycythemia, cardiac failure, hypertension, etc. In Addison's disease BMR is marginally lowered.
10. **Racial variations:** The BMR of Eskimos is much higher.

Significance of BMR: BMR is important to calculate the calorie requirement of an individual and planning of diets. Determination of BMR is useful for the assessment of thyroid function. In hypothyroidism, BMR is lowered (by about 40%) while in hyperthyroidism it is elevated (by about 70%). Starvation and certain disease conditions also influence BMR.

Q. 6. Write a note on caloric values for carbohydrate, fat and proteins.

(TNMGR, March 2007)

Ans. The energy values of the three principal foodstuffs—carbohydrate, fat and protein—measured in a bomb calorimeter and in the body. The carbohydrates and fats are completely oxidized in the body; hence their fuel values, measured in the bomb calorimeter or in the body, are almost the same. Proteins, however, are not completely burnt in the body as they are converted to products such as urea/creatinine and ammonia, and excreted. Due to this reason, calorific value of protein in the body is less than that obtained in a bomb calorimeter. Alcohol is a recent addition to the calorie contribution, as it is a significant dietary component for some people. It must be noted that the nutrients, namely vitamins and minerals, have no calorific value, although they are involved in several important body functions, including the generation of energy from carbohydrates, fats and proteins.

Foodstuff	Energy value (cal/g)	
	In bomb calorimeter	In the body
Carbohydrates	4.1	1
Fat	9.4	9
Protein	5.4	4
Alcohol	7.1	7

Q. 7. Write a note on protein calorie malnutrition.

(TNMGR, March 2009, Oct. 2013)

Ans. Protein calorie energy malnutrition (PCM/PEM) is the most common nutritional disorder of the developing countries. PEM is widely prevalent in the infants and pre-school children. Kwashiorkor and marasmus are the two extreme forms of protein-energy malnutrition.

1. Kwashiorkor: The term kwashiorkor was introduced by Cicely Williams (1933) to a nutritional disease affecting the people of Gold Coast (modern Ghana) in Africa. Kwashiorkor literally means sickness of the deposed child, i.e. a disease the child gets when the next baby is born.

Occurrence and causes: Kwashiorkor is predominantly found in children between 1 and 5 years of age. This is primarily due to insufficient intake of proteins, as the diet of a weaning child mainly consists of carbohydrates.

Clinical symptoms: The major clinical manifestations of kwashiorkor include stunted growth, edema (particularly on legs and hands), diarrhea, discoloration of hair and skin, apathy and moonface, protruding abdomen, dermatitis, subcutaneous fat present.

Biochemical manifestations: Kwashiorkor is associated with a decreased plasma albumin concentration (<2 g/dl against normal 3-4.5 g/dl), fatty liver, deficiency of K⁺ due to diarrhea.

Edema occurs due to lack of adequate plasma proteins to maintain water distribution between blood and tissues. Disturbances in the metabolism of carbohydrate, protein and fat are also observed. Several vitamin deficiencies occur. Plasma retinol binding protein (RBP) is reduced. The immunological response of the child to infection is very low. Serum cortisol may be normal or decreased.

Treatment: Ingestion of protein-rich foods or the dietary combinations to provide about 3-4 g of protein/kg body weight/day will control kwashiorkor.

2. Marasmus: Marasmus literally means "to waste". It mainly occurs in children under one year age. Marasmus is predominantly due to the deficiency of calories. This is usually observed in children given

watery gruels (of cereals) to supplement the mother's breast milk. The symptoms of marasmus include severe growth retardation, muscle wasting (emaciation), anemia and weakness. A marasmic child does not show edema or decreased concentration of plasma albumin. Clinically, the face appears like an old man, abdomen is shrunken, with dry skin, absent subcutaneous fat, increased serum cortisol, normal serum K⁺. Several vitamin deficiencies occur.

4. BIOCHEMICAL INVESTIGATIONS

Q. 1. Discuss the role of various biochemical investigation in dentistry.

(BFUHS, Nov. 2002, 2003; TNMGR, March 2007)

Q. Write about routine blood investigations.

(RGUHS, Nov. 2013)

Q. Discuss the hematological investigations and its normal values.

(BFUHS, 2009)

Ans. Laboratory investigations are extension of the physical examination in which tissue, blood, urine or other specimens are obtained from the patient and subjected to microscopic, biochemical, microbiological or immunologic examination.

In the dental practice, the laboratory investigations are needed for the following reasons:

1. To rule out a suspected condition or disease.
2. To find out an underlying systemic problem.
3. Family history of some diseases which have dental significance.
4. Prior to any major surgical procedure.
5. To confirm any infectious disease.
6. If the physical signs are strongly suggestive of any disease process.

The following factors should be considered before any laboratory investigations:

1. The test should provide meaningful information.
2. Thorough clinical examination should precede any investigation.
3. A negative laboratory report should never be accepted, if there is strong clinical suspicion of any diagnosis.
4. Positive laboratory report may not be conclusive, if the clinical examination are not compatible.
5. The clinician should know the normal values of investigation requested.
6. Simple tests should be carried out first.
7. The laboratory should be provided with adequate of specimen along with patient's details.

Types of laboratory investigations

- a. Screening tests
- b. Diagnostic tests
- c. Prognostic tests

Depending on the nature of laboratory investigations

1. Biopsy: Biopsy refers to the removal of living tissues for the purpose of microscopic examination. The biopsy specimen must be sent to the pathologist without any delay, with complete patient's details. If required, clinical photograph, radiograph should be provided, if required. Local anesthesia should never be injected into the lesion.

Indications

1. To establish a diagnosis in case of suspected malignant lesion.
2. Any chronic nonspecific ulcer.

Contraindications

1. Vascular lesions should not be biopsied on routine basis.
2. Medically compromised patients, acute infections, bleeding disorders.
3. If clinical appearance is suggestive of definitive diagnosis.

Toluidine blue test: This test helps in identifying the site for biopsy. The test is performed by painting the suspected area with 2% toluidine blue vital stain, followed by thorough irrigation with water or rinsing with 1% acetic acid to remove the excess dye.

Chemiluminescence: It refers to emission of light from a chemical reaction. Vizilite is a diagnostic tool used for early detection of cancer is based on this principle.

Types of biopsy

1. Incisional biopsy
2. Excisional biopsy
3. Punch biopsy
4. Aspiration biopsy/needle biopsy
5. Frozen section
6. Oral exfoliative cytology

2. Examination of saliva: Examination of saliva involves flow rate, pH, determination of composition. e.g. salivary calcium level is increased in cystic fibrosis, and asthma. The Na^+/K^+ is high in Addison's disease and low in Cushing's syndrome. Blood group antigens in saliva is important in genetic studies and forensic investigations.

3. Caries activity test: These test mainly provides the information about the individual's susceptibility to

caries in future. These include Snyder test, Lactobacillus, acidophilus count, and salivary buffer capacity.

4. Hematology: Hematology investigation includes evaluation of formed elements as well as determining bleeding and clotting factor deficiency. A complete blood count includes:

- a. Total RBCs count (4–5.4 million cells/ mm^3).
- b. Hemoglobin concentration (12–16 g/dl).
- c. Packed cell volume (40–50%).
- d. *Red cell indices:* Mean corpuscular volume (82–100 μ^3), mean corpuscular hemoglobin concentration (31–37%) and mean corpuscular hemoglobin (26–34 pg).
- e. Total leukocyte count (4000–11000 cells/ mm^3).
- f. *Differential leukocyte count:* Neutrophil (43–77%), lymphocyte (17–47%), monocyte (0–9%), eosinophil (0–4%), and basophil (0–2%).
- g. Peripheral blood smear examination.

Other hematological investigation includes

- a. Erythrocyte sedimentation rate: 0–10 mm/hour.
- b. Platelet count: 1,50,000–4,50,000/ mm^3

5. Tests for bleeding and coagulation disorders

- a. *Capillary fragility test/torniquet test:* This provides information about platelet function. It is positive in vitamin C deficiency.
- b. *Bleeding time:* Normal: 2–6 minute.
- c. *Clotting time:* Normal: 5–10 minute.
- d. Platelet count (1.5–4 lac).
- e. *Clot retraction time:* Normal: Between 2 and 24 hours.
- f. *Prothrombin time (PT):* Normal: 11–15 second.
- g. *Partial thromboplastin time:* Normal: 35–50 second.

6. Serum chemistry

- a. *Plasma proteins:* Normal serum protein level: 6–8 g/dl.
- b. *Calcium:* 9–11 mg/dl.
- c. *Phosphorus:* 2–5 mg/dl.
- d. *Alkaline phosphatase:* 30–110 IU.
- e. *Acid phosphatase:* Elevated levels in metastatic carcinoma of prostate.
- f. *Serum amylase:* Increased in mumps and acute pancreatitis.
- g. *Blood urea nitrogen:* 9–25 mg/dl.
- h. *Uric acid:* 4–8.5 mg/dl.
- i. *Cholesterol:* 160–300 mg/dl.
- j. *Creatinine:* 0.7–1.4 mg/dl.
- k. *Serum sodium, potassium, chloride:* 135–148 mEq/L; 3.5–5.5 mEq/L; 96–110 mEq/L.
- l. *Serum iron, total iron binding capacity:* 55–184 $\mu\text{g}/\text{mm}^3$; 250–425 $\mu\text{g}/\text{mm}^3$.
- m. *Serum enzymes:* SGOT: 8–50 U/L; SGPT: <25 U/L; LDH: 200–400 U/L.

7. Liver function test: Serum bilirubin (0–1.5 mg/dl), urinary urobilinogen (0.1–1.0 Ehrlich units/2 hours), bromsulphalein test (normally <6% dye retention), serum cholesterol, alkaline phosphatase, LDH, and PT.

8. Urinalysis

- Volume:** 1200–1500 ml/24 hours.
- Color:** Light amber.
- pH:** Slightly acidic.
- Specific gravity:** 1.003–1.030.
- Glucose:** 140mg/24 hour.
- Protein:** Normally not present.
- Acetone:** Its presence indicates ketosis.
- Blood:** Hematuria.
- Sediments:** Normally epithelial cells, a few leukocytes, erythrocytes (2–3), bacteria, oxalate, phosphate, and urate crystals.

9. Immunology and serology

- Agglutination test.
- Latex agglutination test.
- Compliment fixation test.
- Heterophile agglutination test (Paul-Bunnell test).
- Monospot test.
- Immunofluorescence test:** Direct, indirect, sandwich technique.
- Diagnosis of syphilis:** Wasserman rection, Kolmer test, Kahn test, reactive plasma reagin test, and VDRL test.

10. Diagnostic skin tests

- Mantoux test:** Used in the diagnosis of tuberculosis.
- Kveim-Siltzbach:** Used in the diagnosis of sarcoidosis.
- Patch tests:** Used in contact dermatitis/stomatitis.

11. Microbiological examination: The microbiological tests includes bacterial smears, cultures and antibiotic sensitivity tests.

12. Examination of the endocrine disorders

- Test for thyroid function:** BMR, protein bound iodine (4–8 mg/dl), butanol-extractable iodine (3–7 mg/dl), triiodothyronine uptake test (11.5–19%), serum thyroxine test (4–11mg/dl), thyroxine binding globulin, pre-albumin, radioactive iodine uptake.
- Test of pancreatic function:** Serum glucose level:
 - Random blood glucose level: 90–120 mg/dl
 - Fasting blood glucose level: 60–90 mg/dl.
 - Postprandial blood glucose level: 110–140 mg/dl.
 - Glucose tolerance test.
 - Glycated hemoglobin test: A value higher than 6.5% indicates diabetes.
 Urine glucose examination.
- Test of parathyroid function.

d. Test of pituitary function.

e. Test of adrenal functions

- Vanillylmandelic acid assay (VMA): 2–10 mg/24 urone sample.
- Urinary 17-hydroxycorticosteroids:** Level decreases in Addison's disease.

13. Nerve and muscle function test

- General sensory perception tests
- Reflex testing
- Autonomic drug tests
- Sweat test of infants nerve conduction test
- Electromyography
- Muscle biopsy
- Blood and urine creatine and creatinine
- Serum creatine phosphokinase
- SGOT
- LDH

Q. 2. Write a short note on liver function test.

(RGUHS, Nov. 2011; TNMGR, Oct. 2012)

Ans. Liver function tests (LFT) are the biochemical investigations to assess the capacity of liver to carry out the functions it performs. LFT will help to detect the abnormalities and extent of liver damage. The major liver tests can be classified as follows:

- Test based on excretory function:** Measurement of bile pigments, bile salts, bromsulphthalein.
- Test based on serum enzymes derived from liver:** Determination of transaminases, alkaline phosphatase, 5'nucleotidase, γ -glutamyltranspeptidase.
- Test based on metabolic capacity:** Galactose tolerance, antipyrine clearance.
- Test based on synthetic functions:** Prothrombin time and Serum albumin.
- Test based on detoxification:** Hippuric acid synthesis.

Q. 3. Write about the investigatory importance of calcium, phosphate and alkaline phosphatase.

(RGUHS, Nov. 2011)

Ans. Alkaline phosphatase (ALP) is mainly derived from bone and liver. A rise in serum ALP (Normal: 3–13 KA units/dl) is usually associated with elevated serum bilirubin is an indicator of biliary obstruction (obstructive jaundice or cholestasis).

ALP is also elevated in cirrhosis of liver and hepatic tumors.

The liver and bone isoenzymes of ALP can be separated by electrophoresis.

An increase in the activity of ALP in plasma is a characteristic feature of rickets. ALP is concerned with the process of bone formation; there is an over-

production of alkaline phosphatase related to more cellular activity of the bone.

It is elevated in certain bone and liver diseases. ALP is useful for the diagnosis of rickets, hyperparathyroidism, carcinoma of bone, and obstructive jaundice isoenzymes of ALP.

As many as six isoenzymes of alkaline phosphatase (ALP) have been identified. ALP is a monomer; the isoenzymes are due to the difference in the carbohydrate content (sialic acid residues). The most important ALP isoenzymes are α_1 -ALP, α_2 -heat labile ALP, α_2 -heat stable ALP, pre- β -ALP, γ -ALP, etc.

Increase in α_2 -heat labile ALP suggests hepatitis whereas pre- β -ALP indicates bone diseases.

Q. 4. Write about laboratory tests for diabetes mellitus. (TNMGR, Sept. 2008)

Q. Write a note on glucose tolerance test. (TNMGR, Oct. 1999)

Ans. The diagnosis of diabetes can be made on the basis of individual's response to the oral glucose load, commonly referred to as **oral glucose tolerance test (OGTT)**.

Preparation of the subject: The person should have been taking carbohydrate-rich diet for at least 3 days prior to the test. All drugs known to influence carbohydrate metabolism should be discontinued (for at least 2 days). He/she should be in an overnight (at least 10 hr) fasting state.

Procedure: A fasting blood sample is drawn and urine collected. The subject is given 75 g glucose orally, dissolved in about 300 ml of water, to be drunk in about 5 minutes. Blood and urine samples are collected at 30 minute intervals for at least 2 hours. All blood samples are subjected to glucose estimation while urine samples are qualitatively tested for glucose.

Interpretation of GTT: The fasting plasma glucose level is 75–110 mg/dl in normal persons. On oral glucose load, the concentration increases and the peak value (140 mg/dl) is reached in less than an hour which returns to normal by 2 hours. Glucose is not detected in any of the urine samples. In individuals with impaired glucose tolerance, the fasting (110–140 mg/dl) as well as 2 hour (140–200 mg/dl) plasma glucose levels are elevated. These subjects slowly develop frank diabetes at an estimated rate of 2% per year. Dietary restriction and exercise are advocated for the treatment of impaired glucose tolerance. A person is said to be suffering from diabetes mellitus if his/her fasting

plasma glucose exceeds 7.8 mmol/L (140 mg/dl) and, at 2 hrs. 11.1 mmol/L (200 mg/dl).

Q. 5. Write a short note on renal function tests. (BFUHS, May 2011)

Ans. The kidney function tests may be divided into four groups:

1. **Glomerular function tests:** All the clearance tests (inulin, creatinine, urea) are included in this group.
2. **Tubular function tests:** Urine concentration or dilution test and urine acidification test.
3. **Analysis of blood/serum:** Estimation of blood urea, serum creatinine, protein and electrolyte are often useful to assess renal function.
4. **Urine examination:** Simple routine examination of urine for volume, pH, specific gravity, osmolality and presence of certain abnormal constituents (proteins, blood, ketone bodies, glucose, etc.) also helps to assess kidney functioning.

Q. 6. Write about the use of blood urea in assessment of kidney function. (TNMGR, March 2007)

Ans. In healthy people, the normal blood urea concentration is 10–40 mg/dl. It is estimated in the laboratory either by urease method or diacetyl monoxime (DAM) procedure. Elevation in blood urea may be broadly classified into three categories:

1. **Pre-renal:** This is associated with increased protein breakdown, leading to a negative nitrogen balance, as observed after major surgery, prolonged fever, diabetic coma, thyrotoxicosis, leukemia and bleeding disorders.
2. **Renal:** In renal disorders like acute glomerulonephritis, chronic nephritis, nephrosclerosis, polycystic kidney, blood urea is increased.
3. **Post-renal:** Whenever there is an obstruction in the urinary tract (e.g. tumors, stones, enlargement of prostate gland, etc.), blood urea is elevated. This is due to increased reabsorption of urea from the renal tubules. The term '**uremia**' is used to indicate increased blood urea levels due to renal failure. **Azotemia** reflects a condition with elevation in blood urea or other nitrogen metabolites which may or may not be associated with renal diseases.

Q. 7. Write a short note on INR. (BFUHS, Oct. 2011)

Ans. International normalized ratio (INR) is the rating of a patient's prothrombin time when compared to an average. It measures extrinsic clotting pathway system. INR is useful in monitoring impact of anticoagulant drugs such as warfarin and to adjust the dosage of

anticoagulants. Patients with atrial fibrillation are usually treated with warfarin to protect against blood clot, which may cause strokes. These patients should have regular blood tests to know their INR in order to adjust warfarin dosage. Blood takes longer time to clot if INR is higher. Normal INR is about 1. In patients taking anticoagulant therapy for atrial fibrillation, INR should be between 2 and 3. For patients with heart valve disorders, INR should be between 3 and 4. But, INR greater than 4 indicates that blood is clotting too slowly and there is a risk of uncontrolled blood clotting.

Q. 8. Write a short note on hyperkalemia.

(TNMGR, April 2000)

Ans. Increase in the concentration of serum potassium is observed in renal failure, adrenocortical insufficiency (Addison's disease), diabetic coma, severe dehydration, intravenous administration of fluids with excessive potassium salts. The manifestations of hyperkalemia include depression of central nervous system, mental confusion, numbness, bradycardia with reduced heart sounds and finally cardiac arrest. Changes in ECG are also observed (elevated T wave).

Q. 9. Write short notes on bilirubinemia.

(TNMGR, Oct. 2000)

Q. Write about classification of jaundice.

(TNMGR, April 2000, Sept. 2002)

Ans. Jaundice (French: Jaune-yellow) is a clinical condition characterized by yellow color of the white of the eyes (sclerae) and skin. It is caused by the deposition of bilirubin due to its elevated levels in the serum. The term hyperbilirubinemia is often used to represent the increased concentration of serum bilirubin.

Classification of Jaundice

1. Hemolytic jaundice: This condition is associated with increased hemolysis of erythrocytes. This results in the overproduction of bilirubin beyond the ability of the liver to conjugate. Hemolytic jaundice is characterized by:

- i. Elevation in the serum unconjugated bilirubin.
- ii. Increased excretion of urobilinogen in urine.
- iii. Dark brown color of feces due to high content of stercobilinogen.

2. Hepatic (hepatocellular) jaundice: This is caused by dysfunction of the liver due to damage to the parenchymal cells. This may be attributed to viral infection (viral hepatitis), poisons and toxins, cirrhosis of liver, cardiac failure, etc. Hepatic jaundice is characterized by:

- i. Increased levels of conjugated and unconjugated bilirubin in the serum.
- ii. Dark-colored urine due to the excessive excretion of bilirubin and urobilinogen.
- iii. Increased activities of alanine transaminases (SGPT) and aspartate transaminase (SGOT) released into circulation due to damage to hepatocytes.
- iv. The patients pass pale, clay-colored stools due to the absence of stercobilinogen.
- v. The affected individuals experience nausea and anorexia (loss of appetite).

3. Obstructive (regurgitation) jaundice: This is due to an obstruction in the bile duct that prevents the passage of bile into the intestine. The obstruction may be caused by gall stones, tumors etc. Due to the blockage in bile duct, the conjugated bilirubin from the liver enters the circulation. Obstructive jaundice is characterized by:

- i. Increased concentration of conjugated bilirubin in serum.
- ii. Serum alkaline phosphatase is elevated as it is released from the cells of the damaged bile duct.
- iii. Dark-colored urine due to elevated excretion of bilirubin and claycolored feces due to absence of stercobilinogen.
- iv. Feces contain excess fat indicating impairment in fat digestion and absorption in the absence of bile (specifically bile salts).
- v. The patients experience nausea and gastrointestinal pain.

4. Jaundice due to genetic defects

i. Neonatal/physiological jaundice: Physiological jaundice is not truly a genetic defect. It is caused by increased hemolysis coupled with immature hepatic system for the uptake, conjugation and secretion of bilirubin. The activity of the enzyme UDP-glucuronyl transferase is low in the newborn. In some infants the serum unconjugated bilirubin is highly elevated, which can cross the blood-brain barrier. This results in hyperbilirubinemic toxic encephalopathy or kernicterus that causes mental retardation. In some neonates, blood transfusion may be necessary to prevent brain damage. Phototherapy deals with the exposure of the jaundiced neonates to blue light. By a process called photoisomerization, the toxic native unconjugated bilirubin gets converted into a non-toxic isomer namely lumirubin. Lumirubin can be easily excreted by the kidneys in the unconjugated form.

- ii. *Crigler-Najjar syndrome type I*: This is also known as congenital nonhemolytic jaundice. It is a rare disorder and is due to a defect in the hepatic enzyme UDP-glucuronyltransferase, the children die within first two years of life.

Q. 10. Write a short note on hemoglobin.

(TNMGR, Sept. 2009)

Ans. Hemoglobin (Hb) is the red blood pigment, exclusively found in erythrocytes. The normal concentration of Hb in blood in males is 14–16 g/dl and in females 13–15 g/dl. Hemoglobin performs two important biological functions concerned with respiration:

1. Delivery of O_2 from the lungs to the tissues.
2. Transport of CO_2 and protons from tissues to lungs for excretion.

Structure of hemoglobin: Hemoglobin (mol. wt. 64,450) is a conjugated protein, containing globin—the apoprotein part and the heme—the non-protein part (prosthetic group). Hemoglobin is a tetrameric allosteric protein.

- Structure of globin:* Globin consists of four polypeptide chains of two different primary structures (monomeric units). The common form of adult hemoglobin (HbA₁) is made up of two β -chains and two α -chains. Each β -chain contains 141 amino acids while α -chain contains 146 amino acids. The four subunits of hemoglobin are held together by non-covalent interactions primarily hydrophobic, ionic and hydrogen bonds. Each subunit contains a heme group.
- Structure of heme:* Heme contains a porphyrin molecule, namely protoporphyrin IX, with iron at its center. Protoporphyrin IX consists of four pyrrole rings to which four methyl, two propionyl and two vinyl groups are attached.

Other forms of hemoglobin

- HbA₂: $\alpha_2\delta_2$
- HbF: $\alpha_2\gamma_2$
- HbA1c: $\alpha_2\beta_2$ -glucose

Q. 11. Write short notes on prostaglandins.

(TNMGR, Oct. 1999)

Ans. Prostaglandins (PGs) are derivatives of a 20-carbon fatty acid, namely prostanoid acid hence known as prostanoids. This has a cyclopentane ring (formed by carbon atoms 8–12) and two side chains, with carboxyl group on one side. Prostaglandins differ in their structure due to substituent group and double bond on cyclopentane ring.

Synthesis: Arachidonic acid is the precursor for most of the prostaglandins in humans. It occurs in the endoplasmic reticulum in the following stages:

1. Release of arachidonic acid from membrane bound phospholipids by phospholipase A₂.
2. Oxidation and cyclization of arachidonic acid to PGG₂ which is then converted to PGH₂ by a reduced glutathione dependent peroxidase.
3. PGH₂ serves as the immediate precursor for the synthesis of a number of prostaglandins, including prostacyclins and thromboxanes.

The above pathway is known as cyclic pathway of arachidonic acid. In the linear pathway of arachidonic acid, leukotrienes and lipoxins are synthesized.

Degradation of prostaglandins: The lung and liver are the major sites of PG degradation.

Biochemical actions: Prostaglandins act as local hormones in their function.

1. *Regulation of blood pressure:* The prostaglandins (PGE, PGA and PGI₂) are vasodilator in function.
2. *Inflammation:* The prostaglandins PGE₁ and PGE₂ induce the symptoms of inflammation (redness, swelling, edema, etc.) due to arteriolar vasodilation.
3. *Reproduction:* PGE₂ and PGF₂ are used for the medical termination of pregnancy and induction of labor.
4. *Pain and fever:* It is believed that pyrogens (fever producing agents) promote prostaglandin biosynthesis leading to the formation of PGE₂ in the hypothalamus. PGE₂ along with histamine and bradykinin cause pain.
5. *Regulation of gastric secretion:* In general, prostaglandins (PGE) inhibit gastric secretion. PGs are used for the treatment of gastric ulcers. However, PGs stimulate pancreatic secretion and increase the motility of intestine which often causes diarrhea.
6. *Influence on immune system:* Macrophages secrete PGE which decreases the immunological functions of B- and T-lymphocytes.
7. *Effects on respiratory function:* PGE is a bronchodilator whereas PGF acts as a constrictor of bronchial smooth muscles.
8. *Influence on renal functions:* PGE increases glomerular filtration rate (GFR) and promotes urine output. Excretion of Na⁺ and K⁺ is also increased by PGE.
9. *Effects on metabolism:* PGE decreases lipolysis, increases glycogen formation and promotes calcium mobilization from the bone.

10. *Platelet aggregation and thrombosis*: The prostaglandins, namely prostacyclins (PGI_2), inhibit platelet aggregation. On the other hand, thromboxane A_2 (TXA_2) and prostaglandin E_2 promote platelet aggregation and blood clotting that might lead to thrombosis. PGI_2 prevents the adherence of platelets to the blood vessels. TXA_2 is released by the platelets and is responsible for their spontaneous aggregation when the platelets come in contact with foreign surface, collagen or thrombin. In the overall effect PGI_2 acts as a vasodilator, while TXA_2 is a vasoconstrictor.

Q. 12. Write short notes on inborn errors in tyrosine metabolism. (TNMGR, Oct. 2003)

Ans. Several enzyme defects in phenylalanine/tyrosine degradation leading to metabolic disorders are known.

1. Phenylketonuria: Phenylketonuria (PKU) is the most common metabolic disorder in amino acid metabolism. It is due to the deficiency of the hepatic enzyme, phenylalanine hydroxylase, caused by an autosomal recessive gene. This enzyme deficiency impairs the synthesis of tetrahydrobiopterin required for the action of phenylalanine hydroxylase. The net outcome in PKU is that phenylalanine is not converted to tyrosine. Due to disturbances in the routine metabolism, phenylalanine is diverted to alternate pathways, resulting in the excessive production of phenylpyruvate, phenylacetate, phenyllactate and phenylglutamine. All these metabolites are excreted in urine, in high concentration in PKU. Phenylacetate gives the urine, a mousey odor.

Biochemical manifestations

- i. *Effects on central nervous system (CNS)*: Mental retardation, failure to walk or talk, failure of growth, seizures and tremor are the characteristic findings in PKU. If untreated, the patients have very low IQ (below 50).
- ii. *Effect on pigmentation*: Accumulation of phenylalanine competitively inhibits tyrosinase and impairs melanin formation. The result is hypopigmentation that causes light skin color, fair hair, blue eyes, etc.

Diagnosis: PKU is mostly detected by screening the newborn babies for the increased plasma levels of phenylalanine (PKU, 20–65 mg/dl; normal 1–2 mg/dl).

Treatment: The maintenance of plasma phenylalanine concentration within the normal range is the main target for management. This is done by selecting foods with low phenylalanine content and/or feeding synthetic amino acid preparations, low in phenylalanine. In seriously affected PKU patients, treatment includes

administration of 5-hydroxytryptophan and dopa to restore the synthesis of serotonin and catecholamines.

2. Tyrosinemia type II: This disorder also known as **Richner-Hanhart syndrome**, is due to a defect in the enzyme tyrosine transaminase. The result is a blockade in the routine degradative pathway of tyrosine. Accumulation and excretion of tyrosine and its metabolites, p-hydroxyphenylpyruvate, p-hydroxyphenyllactate, p-hydroxyphenylacetate, N-acetyltyrosine and tyramine are observed. Tyrosinemia type II is characterized by skin (dermatitis) and eye lesions, and rarely, mental retardation.

3. Neonatal tyrosinemia: The absence of the enzyme p-hydroxyphenylpyruvate dioxygenase causes neonatal tyrosinemia. This is mostly a temporary condition and usually responds to ascorbic acid.

4. Alkaptonuria (black urine disease): Alkaptonuria is an autosomal recessive disorder, defective enzyme is homogentisate oxidase in tyrosine metabolism. Homogentisate accumulates in tissues and blood and is excreted into urine. Homogentisate, on standing, gets oxidized to give black or brown color (coke in color urine).

Biochemical manifestations: Oxidized product of homogentisate, alkapton, gets deposited in connective tissue, bones and various organs (nose, ear, etc.) resulting in a condition known as **ochronosis**. Many alkaptonuric patients suffer from arthritis, due to the deposition of pigment alkapton (in the joints).

Diagnosis: Change in color of the urine on standing to brown or dark has been the simple traditional method to identify alkaptonuria. The urine gives a positive test with ferric chloride and silver nitrate. Benedict's test—employed for the detection of glucose and other reducing sugars, is also positive with homogentisate.

Treatment: Alkaptonuria does not require any specific treatment. However, consumption of protein diet with relatively low phenylalanine content is recommended.

5. Tyrosinosis or tyrosinemia type I: This is due to the deficiency of the enzymes fumarylacetoacetate hydroxylase and/or maleylacetoacetate isomerase. It causes liver failure, rickets, renal tubular dysfunction and polyneuropathy. Tyrosine, its metabolites and many other amino acids are excreted in urine. In acute tyrosinosis, the infant exhibits diarrhea, vomiting, and 'cabbage-like' odor. Death may occur due to liver failure within one year. For the treatment, diets low in tyrosine, phenylalanine and methionine are recommended.

6. Albinism: Albinism is an inborn error, due to the lack of synthesis of the pigment melanin. It is an

autosomal recessive disorder with a frequency of 1 in 20,000. The most common cause of albinism is a defect in tyrosinase, the enzyme most responsible for the synthesis of melanin.

Clinical manifestations: Lack of melanin in albinos makes them sensitive to sunlight. Increased susceptibility to skin cancer (carcinoma) is observed. Photophobia (intolerance to light) is associated with lack of pigment

in the eyes. However, there is no impairment in the eyesight of albinos.

7. Hypopigmentation: Hypopigmentation disorders may be either diffuse or localized. A good example of diffuse hypopigmentation is oculocutaneous albinism which is mostly due to mutations in the tyrosinase gene. Vitiligo and leukoderma are the important among the localized hypopigmentation disorders.

1. IMMUNITY

Q. 1. Write a note on acquired immunity.

(TNMGR, April 1995; UHSR, April 2015)

Q. Write a short note on passive immunity.

(TNMGR, April 2000)

Ans. The resistance that an individual acquire during life is known as acquired immunity as distinct from inborn innate immunity.

Acquired immunity is of two types

- a. **Active immunity/adaptive immunity:** The resistance developed by an individual as a result of an antigenic stimulus, which involves the active functioning of the host's immune apparatus, by the formation of antibodies and the immunologically active cells. This develops only after a latent period, once developed it is long-lasting. The secondary response is quicker, abundant. This has immunological memory, more effective and has better protection.
- b. **Passive immunity:** The resistance that is transmitted passively to a recipient in a 'ready-made' form. The recipient's immune system plays no active role, as preformed antibodies are administered. There is no latent period, and the protection being effective immediately after passive immunization. The immunity is transient, usually lasting for days or weeks. No secondary response occurs and this is less effective in protection.

Active immunity may be natural or artificial

1. **Natural active immunity:** Results from either a clinical or an in apparent infection by a microbe. Such immunity is usually long-lasting but the duration varies with the type of pathogen. The immunity following bacterial infection is generally less permanent than that of following viral infections.

2. **Artificial active immunity:** It is the resistance induced by vaccines. Vaccines are preparations of live or killed microorganisms or their products used for immunization. Examples:

- i. **Bacterial vaccines**
 - a. Live (BCG vaccine for tuberculosis)
 - b. Killed (cholera vaccine)
 - c. Subunit (typhoid Vi antigen)
 - d. Bacterial products (tetanus toxoid)
- ii. **Viral vaccines**
 - a. Live (oral polio vaccine—sabin)
 - b. Killed (injectable polio vaccine—salk)
 - c. Subunit (hepatitis B vaccine)

Natural passive immunity: It is the resistance passively transferred from mother to baby. In human infants, maternal antibodies are transmitted predominantly through the placenta.

Artificial passive immunity: It is the resistance passively transferred to a recipient by the administration of antibodies. The agents used are hyperimmune sera, convalescent sera and pooled human gamma globulin. These are used for the prophylaxis and therapy. Passive immunization is indicated for immediate and temporary protection in a non-immune host faced with the threat of an infection, when there is insufficient time for active immunization to take effect. It is also indicated for the treatment of some infections.

Q. 2. Write a short note on immunoglobulins.

(Bombay Uni., Oct. 1985; TNMGR, Sept. 2008; March 2011)

Ans. The generic term immunoglobulin was internationally accepted for proteins of animal origin endowed with known antibody activity and for certain other proteins related to them by chemical structure (WHO). Based on physiochemical and antigenic

differences, five classes of immunoglobulins have been recognized—IgG, IgA, IgM, IgD and IgE.

1. **IgG:** Major serum immunoglobulin (80%). It has molecular weight of 150,000 (7s). It has half-life of approximately 23 days. IgG is the only maternal immunoglobulin that is normally transported across the placenta. It is not synthesized by the fetus. It binds to microorganisms and enhances their phagocytosis and participates in complement fixation, precipitation, and neutralization of toxins and viruses. Four sub-classes of IgG have been recognized (IgG1, IgG2, IgG3, IgG4), each possessing a distinct type of gamma chain, identifiable with specific antisera.
2. **IgA:** Second most abundant (10–13%). Its half life is 6–8 days. It is the major immunoglobulin in the colostrum, saliva and tears. It occurs in two forms—**serum IgA** and **secretory IgA**.
3. **IgM:** It constitutes 5–8 percent of serum immunoglobulins. It has half life about 5 days. It is a heavy molecule hence called the millionaire molecule. Its presence indicates recent infection. It is the major antibody receptor on the surface of B-lymphocytes.
4. **IgD:** It resembles IgG structurally. It is mostly intravascular. It has half life of about 3 days. It occurs on the surface of unstimulated B-lymphocytes.
5. **IgE:** Its half life is 2 days, resembles to IgG, heat labile, mostly extravascular. It is chiefly produced in the lining of the respiratory and intestinal tracts. It is responsible for the anaphylactic type of hypersensitivity.

Q. 3. Define antigen and antibody. What are the antigen–antibody reactions? Add a note on the human complement system. (TNMGR, March 2009)

Ans. An **antigen** is defined as any substance, which when introduced parenterally into the body, stimulates the production of an antibody with which it reacts specifically and in an observable manner. The substances thus produced from serum and tissue fluids, on introduction of antigen into the body are known as **antibody**.

Antigen–antibody reactions: These reactions form the basis of antibody mediated immunity in infectious diseases or in tissue injury. These reactions can be used for the detection and quantification of either antigen or antibodies. These reactions occur in three stages:

Primary stage: The initial reaction between the antigen–antibody, without any visible effect. The reaction is rapid, reversible, can be detected by use of markers such as radioactive isotopes, fluorescent dyes or ferritin.

Secondary stage: This is the stage of demonstrable event such as precipitation, agglutination, lysis of cells, killing of live antigens, neutralization of toxins, fixation of complement and enhancement of phagocytosis.

Tertiary reactions: Chain of reactions leading to neutralization or destruction of injurious antigens or to tissue damage. These include humoral immunity against infectious diseases, clinical allergy and immunological diseases.

Features of antigen–antibody reactions

1. The reaction is specific.
2. Entire molecule react and not the fragments.
3. There is no denaturation of antibody or antigen.
4. The combination occurs at the surface.
5. The combination is firm but reversible.
6. Both antigens and antibodies participate in the formation of agglutinates or precipitates.
7. Antigens and antibodies can combine in varying proportions.

Types of Antigen–antibody Reactions

- a. *Precipitation or flocculation reaction*
 1. Ring test
 2. Slide test
 3. Tube test
 4. Immunodiffusion
 5. Electroimmunodiffusion
- b. *Agglutination reaction*
 1. Slide agglutination
 2. Tube agglutination
 3. Antiglobulin (Coombs') test
 4. Passive agglutination test
- c. *Complement fixation test*
 1. Indirect complement fixation test
 2. Conglutinating complement absorption test
 3. Immobilization test
- d. *Neutralization test*
 1. Virus neutralization test
 2. Toxin neutralization test
- e. Opsonization
- f. *Immunofluorescence*
 1. Direct immunofluorescence
 2. Indirect immunofluorescence
- g. Radioimmunoassay
- h. Enzyme immunoassays—ELISA
- i. Chemiluminescence immunoassay
- j. Immunoelectroblot techniques
- k. Immunochromatographic tests

1. *Immunoelectromicroscopic tests*
 1. Immunoelectromicroscopy.
 2. Immunoferritin test.
 3. Immunoenzyme test.

Human complement system: Complement refers to a system of factors which occur in a normal serum and are activated characteristically by antigen-antibody interaction and subsequently mediate a number of biological consequences.

Properties

1. Complement is present in all the mammals.
2. Complement as a whole is heat labile.
3. It does not bind to free antigen or antibody.
4. The fixation of complement is not influenced by nature of antigens.

Components: It is a complex of nine different fractions called C1 to C9.

Activation: It is activated by series of reactions:

1. Classical pathway
2. Alternative or properdin pathway

Inhibitors

1. C1 esterase.
2. S protein.

Biological effects

1. It mediates immunological membrane damage.
2. It amplifies the inflammatory response.
3. Participates in pathogenesis of hypersensitivity reactions.
4. It exhibits antiviral activity.
5. It interacts with coagulation, kinin and fibrinolytic system.

Q. 4. Write a short note on defense mechanism of the body. (TNMGR, March 2010)

Q. Write a short note on defense mechanism of the oral cavity. (RGUHS, April 2007)

Ans. The major components of defense mechanism are:

A. Local Defenses

1. **Epithelial lining:** Lining epithelial cells physically hinders the penetration of surface bacteria into deeper tissue. This mechanical function is enhanced by keratin of skin and secretory and drainage capabilities of mucous membrane. Epidermal cells release a variety of cytokines which assist in local defenses.

2. **Antimicrobial peptide:** These peptides are synthesized by epithelial cells; with cationic and hydrophobic properties they disrupt the phospholipid bilayer of microbes. They are antibacterial, antifungal, antiviral and antitumor and antitoxic effects. For example, defensins, histatins, bacteriocins.
3. **Secretion and drainage system:** The mucocilliary activity, peristaltic motion, and flushing action results in drainage and mechanical removal of bacteria.
4. **Microbial interference:** It refers to the inhibitory effect exerted by one microorganism on the growth and proliferation of another. This occurs by production of bacteriocins, interference with microbial binding to epithelium, competition for nutrients.
5. **Mucosal immune system:** The immunoglobulins in secretions, along with other local protective factors constitute an important first line defense.

B. Humoral Defenses

1. **Immunoglobulins:** The host on antigenic stimulation synthesizes immunoglobulins, which have antibody activity. They are derived from sensitized B lymphocytes or plasma cells.
2. **Complement system:** It consists of group of serum proteins, that produces and release by-products initiating inflammatory reactions, regulating and enhancing phagocytic functions and attacking bacterial cell membrane.

C. Cellular Components

If the invading microbe escapes the first line of defense, provided by the local and humoral factors, then cellular components like phagocytes and lymphocytes come into play. Their activation requires binding of the signal or ligand to a cell surface receptor. Formation of the signal-receptor complex then is followed a cascade of reactions that eventually result in translation of signal to cell function.

Defense mechanism of the oral cavity: Homeostasis in the oral cavity is maintained by the innate and acquired immune system in conjunction with normal oral flora and intact oral mucosa. Components contributing to oral defense include saliva, salivary antimicrobial proteins, gingival crevicular fluid, transudating plasma proteins, circulating WBCs, oral mucosal keratinocyte products and proteins from microbial flora. Mucosal integrity prevents penetration of microorganism and macromolecules in the diet and environment that might be antigenic. The crown of the tooth is protected from caries by salivary secretions.

Q. 5. Write a short note on hypersensitivity reactions.

(TNMGR, March 2007; Oct. 2012)

Ans.

1. **Type I (anaphylactic, IgE or reagin dependent):** IgE antibodies are fixed on the surface of tissue cells (mast cells and basophils) in the sensitized individuals, to which the antigen combines, leading to release of vasoactive amines, which produces the clinical reaction, e.g. anaphylaxis and atopy.
2. **Type II (cytotoxic or cell stimulating):** IgG or IgM antibodies react with the cell surface or tissue antigens. Cell or tissue damage occurs in the presence occurs in the presence of complement or mononuclear cells, e.g. antibody mediated thrombocytopenia, agranulocytosis, hemolytic anemia, etc.
3. **Type III (immune complex or toxic complex diseases):** The damage is caused by antigen antibody complexes. For example, arthus reaction and serum sickness.
4. **Type IV (delayed or cell mediated):** The antigen activates specifically sensitized CD4, CD8 T cells, leading to the secretion of lymphokines, with fluid and phagocyte accumulation.

Q. 6. Write a short note on type I hypersensitivity reaction.

(TNMGR, April 1998)

Q. Write a short note on anaphylactic reaction.

(TNMGR, Oct. 2000; RGUHS, Nov. 2011)

Ans. These occur in two forms

1. The acute, potentially fatal, systemic form called **anaphylaxis**.
2. The chronic or recurrent, nonfatal, typically localized form called **atopy**.

Anaphylaxis: The term anaphylaxis (ana: without, phylaxis: protection) was coined by Richet (1902). The clinical effects are due to smooth muscle contraction and increased vascular permeability. Tissues or organs predominantly involved in the anaphylactic reaction are known as '**target tissues**' or '**shock organs**'. Other changes seen in anaphylaxis are edema, decreased coagulability of blood; fall in blood pressure and temperature, leucopenia and thrombocytopenia. In human beings, fatal anaphylaxis is rare.

Symptoms and signs

1. Itching of the scalp and tongue
2. Flushing of the skin over the whole body
3. Difficulty in breathing
4. Nausea
5. Vomiting
6. Abdominal pain

7. Diarrhea
8. Blood in the stool
9. Acute hypotension
10. Loss of consciousness and death

Causes: Injections of antibiotics or other drugs, insect stings.

Treatment: Adrenaline is to be administered 0.5 ml of a 1 in 1000 solution, subcutaneously or intramuscularly; the dose being repeated up to a total of 2 ml over 15 minutes, if necessary.

Mechanism: The immunologic basis for hypersensitivity is cytotoxic IgE antibody, which binds to cells, releasing their granules, which acts as pharmacological mediators:

- i. **Primary mediators of anaphylaxis:** Pre-formed contents of mast cell and basophil granules (histamine, serotonin, eosinophil, chemotactic factor of anaphylaxis, neutrophil chemotactic factor, heparin and various proteolytic enzymes).
- ii. **Secondary mediators:** Newly formed upon stimulation by mast cells, basophils and other leukocytes. For example, slow reacting substance of anaphylaxis, prostaglandins, platelet activating factor and cytokines.

Anaphylactoid reaction: Intravenous injection of peptone, trypsin and certain other substances provokes a clinical reaction resembling anaphylactic shock. This is termed '**anaphylactoid reaction**.' The clinical resemblance is due to the same chemical mediators participating in both reactions. The only difference is that anaphylactoid shock has no immunological basis and is a nonspecific mechanism involving the activation of complement and the release of anaphylatoxins.

Atopy: The term 'atopy' refers to naturally occurring familial hypersensitivities of human beings, typified by hay fever and asthma. The antigens commonly involved in atopy are characteristically inhalants (pollen, house dust) or ingestants (egg, milk). Predisposition to atopy is genetically determined, probably linked to major histocompatibility complex (MHC) genotype. Atopy therefore runs in families. Atopic sensitivity is due to an overproduction of IgE antibodies, often associated with a deficiency of IgA. The symptoms of atopy are caused by the release of pharmacologically active substances following the combination of the antigen and the cell fixed IgE. The clinical expression of atopic reactions is usually determined by the portal of entry of the antigen—conjunctivitis, rhinitis, gastrointestinal symptoms and dermatitis following exposure through the eyes, respiratory tract, intestine or skin respectively.

Q. 7. Write a note on type III hypersensitivity reaction.
(TNMGR, Oct. 2003)

Q. Discuss the importance of immune complexes (autoimmune) in dental diseases. (TNMGR, Oct. 1999; April 2012)

Ans. Type III hypersensitivity reactions (immune complex or toxic complex disease): In this the damage is caused by antigen-antibody complexes. These may precipitate in and around small blood vessels, causing damage to cells secondarily, or on membranes, interfering with their function.

1. **Arthus reaction:** It is a local manifestation of generalized hypersensitivity, in which the tissue damage is due to formation of antigen-antibody precipitates causing complement activation and release of inflammatory molecules. This leads to increased vascular permeability and infiltration of the site with neutrophils. Leukocyte-platelet thrombi are formed that reduce the blood supply and lead to tissue necrosis. For example, farmer's lung.

2. **Serum sickness:** This is a systemic form of type III hypersensitivity. The clinical syndrome consists of fever, lymphadenopathy, splenomegaly, arthritis, glomerulonephritis, endocarditis, vasculitis, urticarial rashes, abdominal pain, nausea and vomiting, appearing 7-12 days following injection. The pathogenesis is the formation of immune complexes which get deposited on the endothelial lining of blood vessels in various parts of the body, causing inflammatory infiltration. The plasma concentration of complement falls due to massive complement activation and fixation by the antigen antibody complexes. The disease is self-limited. With continued rise in antibody production the immune complexes become larger and more susceptible to phagocytosis and immune elimination. Serum sickness differs from other types of hypersensitivity reaction in that a single injection can serve both as the sensitizing dose and the shocking dose. Immune complexes occur in many diseases, including bacterial, viral and parasitic infections (e.g. post-streptococcal glomerulonephritis, hepatitis type B, and malaria), disseminated malignancies and autoimmune conditions.

Q. 8. Write a note on delayed hypersensitivity.
(TNMGR, April 2013)

Ans. It is type IV hypersensitivity reaction, provoked by intracellular microbial infections or haptens, evolve slowly and consist of mixed cellular reactions involving lymphocytes and macrophages. This reaction is induced by sensitized T cells, which releases cytokines.

Two types

1. **Tuberculin (infection) type:** When a small dose of tuberculin is injected intradermally in a sensitized individual, an indurated inflammatory reaction develops at the site within 48-72 hours. It provides useful indication of cell mediated immunity to the bacilli.

2. **Contact dermatitis type:** This type of reaction develops when allergen come in contact of skin of sensitized individual. The lesions vary from macules and papules to vesicles. Hypersensitivity is determined by patch test.

2. MICROFLORA OF ORAL CAVITY

Q. 1. Write a short note on oral microbial flora.

(Bangalore Uni., Jan. 1992; TNMGR, Sept. 2010; April 2012; RGUHS, Nov. 2011)

Ans. The mouth contains plethora of organism—pigmented and nonpigmented cocci, some of which are aerobic, gram-positive aerobic spore bearing bacilli, coliforms, proteus and lactobacilli.

The gum pockets and the crypts of tonsils have anaerobic micrococci, microaerophilic and anaerobic streptococci, vibrios, fusiform bacilli, *Corynebacterium* species, *Actinomyces*, *Leptothrix*, *Mycoplasma*, *Neisseria* and bacteriophage.

The mouth of infant contains mixture of micrococci, streptococci, coliform bacilli; Doderlien's bacilli. *S. salivarius* is present early in infants. *S. sanguis* appear only after the eruption of teeth. Anaerobic fusiform bacilli found in infants mouths younger than 2 months and before eruption of incisors. Fusiform bacilli increase in number during 4-8 months. *Peptostreptococcus* appears in 5 months old infants.

The mouth of 1-year-old child contains streptococci, staphylococci, neisseriae and veillonella. Less commonly are lactobacilli, *Actinomyces*, *Prevotella*, *Fusobacteria*, *Nocardia*, *Candida*, *Bacteroides*, *Corynebacterium*, *leptotrichia* and coli form types.

In adolescence with the eruption of permanent teeth there is increase in the anaerobic forms like *Bacteroides*, *leptotrichia*, *fusobacteria*, and *spirochetes* and *Vibrio*.

Q. 2. Write a note on microbiology of dental caries.

(TNMGR, April 1998, 2001; Oct. 2013; MUHS, May 2012)

Q. Why dental caries is infectious and transmissible disease?
(TNMGR, April 2012)

Ans. The microflora of dental caries is gram-positive bacteria, facultative aerobic bacteria and later on, when

the lesion depth increases anaerobic and proteolytic bacteria appear. In the process of dental caries initiation, *S. mutans* have been implicated, whereas lactobacillus is implicated in caries progression.

Types of caries	Microorganism
Pit and fissure	Mutans streptococci, <i>S. sanguis</i> , lactobacilli species, Actinomyces species
Smooth surface	Mutans streptococci, <i>S. salivarius</i>
Root surface	<i>A. viscosus</i> , <i>A. naesulundi</i> , mutans streptococci
Deep dentinal caries	Lactobacilli species, <i>A. naesulundi</i> , other filamentous rods

Q. 3. Write a short note on gram-positive cocci.

(TNMGR, April 2013)

Ans.

Gram-positive cocci	Location
<i>Staphylococcus aureus</i>	Oral cavity, pharynx
<i>Staphylococcus epidermidis</i>	Oral cavity, pharynx, skin
<i>Streptococcus mitis</i>	Oral cavity, oropharynx
<i>Streptococcus oralis</i>	Oral cavity, oropharynx
<i>Streptococcus parasanguis</i>	Oral cavity, oropharynx
<i>Streptococcus sanguis</i>	Oral cavity
<i>Streptococcus pneumoniae</i>	Upper respiratory tract
<i>Salivarius salivarius</i>	Oral cavity, especially saliva and tongue
<i>Salivarius vestibularis</i>	Oral cavity, especially vestibular mucosa
<i>Anginosus anginosus</i>	Oral cavity, upper respiratory tract, vagina
<i>Anginosus mutans</i>	Dental plaque, carious tooth
<i>Gemella morbillorum</i>	In peridontium
<i>Streptococcus pyogenes</i>	Oropharynx of neonates
<i>Enterococcus spp.</i>	Oral cavity and intestine

Q. 4. Write a short note on *Streptococcus viridans*.

(TNMGR, March 2008)

Ans. This group, is a miscellany of streptococci normally resident in the mouth and upper respiratory tract, and typically producing greening (alpha lysis) on blood agar hence the name viridans. Some of them may be nonlytic. They cannot be categorized under the Lancefield antigenic groups. They are ordinarily non-pathogenic but can on occasion cause disease. In persons with pre-existing cardiac lesions, they may cause bacterial endocarditis, *S. sanguis* being most often responsible. Following tooth extraction or other dental procedures, they cause transient bacteremia and get implanted on damaged or prosthetic valves or in a

congenitally diseased heart, and grow to form vegetations. Prophylactic antibiotic cover is advisable in such persons before tooth extraction or similar procedures, while viridans streptococci are generally penicillin sensitive, some strains may be resistant. It is therefore essential that in endocarditis, the causative strain is isolated and its antibiotic sensitivity determined so that appropriate antibiotics in adequate bactericidal concentration can be employed for treatment. *S. mutans* (so called because it assumes a bacillary form in acid environments) is important in the causation of dental caries. It breaks down dietary sucrose, producing acid and a tough adhesive dextran. The acid damages dentine and the dextran bind together food debris, epithelial cells, mucus and bacteria to form dental plaques, which lead to caries. Experimental caries in monkeys has been prevented by a *S. mutans* vaccine, but its extension to human use is fraught with problems.

Q. 5. Write a short note on *Streptococcus mutans*.

(TNMGR, March, 2007; April 2011)

Ans. They are gram-positive cocci, catalase negative, forming short to medium chains on mitis salivarius agar; they grow in highly convex colonies. Characteristically, *S. mutans* synthesize insoluble polysaccharides from sucrose. It is homofermentive and more aciduric than other streptococci. Cariogenic strains contain lysogenic bacteriophage. *S. mutans* does not colonize the mouth of infants prior to the eruption of teeth. It disappears from the mouth after complete extraction of teeth. Infants get infected from their parents. Based on nucleic acid-base content, it has been divided into five genotypes: *S. mutans*, *S. rattus*, *S. sobrinus*, *S. cricetus*, *S. ferus*. *S. mutans* have been divided into eight serotypes 'a' to 'h'. The specific antigen for each serotype represents cell wall constituents, which are chemically characterized as polysaccharides. It utilizes sucrose for its energy requirements and results in formation of lactic acid.

Q. 6. Write a note on microbiology of wound infection.

(TNMGR, March 2002)

Ans. Most wound infections manifest within a week of surgery. *Strep. pyogenes* and clostridial infections appear within 1–2 days. Staphylococcal infections typically take 4–5 days. Gram-negative bacillary take 6–7 days.

Nonsurgical sites of wound infections include infection cut down, umbilical stumps, ulcers and burns. *Pseudomonas aeruginosa* is the most important cause of infection in burns.

Q. 7. Write a note on microflora in infected root canal.

(RGUHS, Nov. 2011)

Ans. The root canal flora is dominated by anaerobic bacteria.

1. **Anaerobic gram-negative bacteria:** Treponema, Porphyromonas, Fusobacterium, Prevotella, Veillonella.
2. **Facultative gram-negative bacteria:** Neisseria, Capnocytophaga, Haemophilus.
3. **Anaerobic gram-positive bacteria:** Actinomyces, Eubacterium, Propionibacterium, Peptostreptococcus.
4. **Facultative gram-positive bacteria:** Enterococcus, Actinomyces, Streptococcus, Lactobacillus.

Q. 8. Write about *Enterococcus faecalis* and its significance.

(TNMGR, Sept. 2010)

Ans. *E. faecalis* plays a major role in the etiology of persistent periapical lesions after root canal treatment. It is commonly found as a major flora of root canals. It is more commonly associated with asymptomatic cases than symptomatic cases. It can endure prolonged periods of nutritional deprivation. It binds to dentin and invades the dentinal tubules. It alter host response, suppresses the action of lymphocytes. It possesses lytic enzymes, cytolysin, aggregation substance, pheromones. It utilizes serum as a nutritional source. It resists the intracanal medicaments, competes with other cells and forms a biofilm.

Q. 9. Write a short note on endodontic biofilm.

(TNMGR, April 2015)

Ans. Biofilm is defined as a community of microcolonies of microorganisms in an aqueous solution that is surrounded by a matrix made of glycocalyx. A biofilm has following features—autopoiesis, homeostasis, synergy, communality. They are significant as they are responsible for endodontic failure, because of their ability to protect the bacteria.

Classification

1. Intracanal microbial biofilms
2. Extra-radicular microbial biofilms
3. Periapical microbial biofilms

Q. 10. Write about role of anaerobic microorganism in maxillofacial infection.

(TNMGR, Sept. 2008)

Q. Write a short note on anaerobic microorganism.

(RGUHS, Oct. 2010)

Ans.**Gram-negative rods**

Bacteroides spp.	Peridontium
Fusobacterium spp.	Peridontium
Porphyromonas spp.	Peridontium, oral cavity
Prevotella spp.	Peridontium, periodontal and endodontic lesions
<i>Centipeda periodonti</i>	Peridontium
<i>Leptotrichia buccalis</i>	Oral mucosa
Selenomonas spp.	Peridontium

Gram-negative cocci

Veillonella spp.	Tongue and saliva
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Gram-positive rods

Actinomyces spp.	Dental plaque, calculus
<i>Bifidobacterium dentium</i>	Dental plaque
Eubacterium spp.	Gingival tissues

Gram-positive cocci

<i>Peptococcus niger</i>	Subgingival areas
<i>Peptostreptococcus</i> spp.	Subgingival areas

3. BACTERIOLOGY**Q.1 Add a note on different culture media and methods.**

(TNMGR, March 2008)

Ans.**A. Culture media**

1. Solid, liquid, semisolid media.
2. Simple (nutrient broth, nutrient agar), complex, defined media, semidefined media (simple peptone water medium), special media (enriched: blood agar; enrichment: tetrathione broth; selective: desoxycholate citrate medium; differential: MacConkey's medium; sugar, transport media: Stuart's medium).
3. Aerobic and anaerobic media: Robertson's cooked meat medium.

B. Culture Methods

1. Streak culture method
2. Lawn or carpet method
3. Stroke culture method
4. Stab culture method
5. Pour plate method
6. Liquid culture method

Q. 2. Write a short note on anaerobic culture methods.

(TNMGR, March 2002, April 2012, 2013)

Ans. Methods of achieving anaerobiosis

1. Incubating cultures in vacuum desiccators.
2. Displacement of oxygen with gases such as hydrogen, nitrogen, helium, or carbon dioxide by use of candle jar.

3. **Chemical method:** By using alkaline pyrogallol which adsorbs oxygen, by using mixture of chromium and sulphuric acid (Rosenthal method), by using yellow phosphorus.
4. **Biological methods:** By incubating with aerobic bacteria, germinating seeds or chopped vegetables. (Most reliable and widely used method is McIntosh-Fildes anaerobic jar).
5. **By using reducing agents:** Such as 1% glucose, 0.1% thioglycolate, 0.1% ascorbic acid and 0.05% cysteine.
6. Robertson's cooked meat medium.

Q. 3. Write a short note on mechanism of drug resistance. (TNMGR, Sept. 2002)

Q. Write a short note on microbial resistance and its clinical relevance. (TNMGR, April, 2013)

Ans. The bacteria acquire drug resistance by:

1. Mutational resistance

- a. **Stepwise mutation:** Resistance is achieved by series of stepwise mutation, as seen with the penicillin.
- b. **One step mutation:** Mutants differ widely in the resistance as seen with the streptomycin.

2. Genetic transfer resistance

- a. **Transduction:** Transfer of portion of DNA from one bacterium to another by a bacteriophage is known as transduction.
- b. **Resistance transfer factor (RTF):** Resistance is plasmid mediated and transferred by conjugation. The whole plasmid [RTF + resistance determinant(r)] is known as R factor, which is the most important mechanism of drug resistance.

Q. 4. Write a short note on Vincent's organism. (TNMGR, April 1995)

Q. Write a short note on Vincent's angina. (TNMGR, Oct. 1999; Aug. 2004)

Ans. *Borrelia* (*Treponema*) *vincenti* is called as Vincent's organism. It forms symbiotic combination with the fusiform bacillus. It is motile spirochete, which is longer and coarser than the treponemes. It is about 5–20 µm long and 0.2–0.6 µm wide with 3–8 coils of variable size. It is easily stained with dilute carbol fuchsin and is gram-negative. It is a normal mouth commensal but, under predisposing conditions such as malnutrition or viral infections, gives rise to ulcerative gingivostomatitis or oropharyngitis (Vincent's angina). It is an opportunistic disease. It is also called fusospirochetal disease because *Fusobacterium fusiforme* is always associated with it.

Transmission: It is generally not transmissible through direct contact. The infection is usually endogenous and

its source is patient's own mouth. However, the epidemics noted during First World War, when it was known as trench mouth. It spreads due to poor dental hygiene, poor nutrition in susceptible individual.

Laboratory diagnosis: Smears are made directly from the ulcerative lesions and stained with dilute carbol-fuchsin. Clinical diagnosis is confirmed when large number of both spirochetes and fusiform bacilli are seen along with pus cells.

Treatment: Penicillin is the drug of choice. Tetracycline and metronidazole are also effective.

Q. 5. Write a short note on acute ulcerative gingivitis. (TNMGR, March 2007)

Ans. This is an acute, ulcerative, inflammatory condition of gingiva, associated with polymicrobial infection. Predisposing factors include immunosuppression, debilitation, smoking, stress, poor oral hygiene, local trauma, contaminated food supply, and diabetes.

Etiology and pathogenesis: *Treponema* spp., *Prevotella intermedia*, *Fusobacteria nucleatum*, *Peptostreptococcus micros*, *Porphyromonas gingivalis*, *Campylobacter*. The tissue destruction is mostly due to production of endotoxins. There is also reduced neutrophil chemotaxis and phagocytosis, resulting in poor infection control.

Clinical features: High grade fever, malaise, regional lymphadenopathy, excessive salivation, metallic taste, sensitivity of gingiva, extremely painful erythematous gingiva with punched out ulceration of interdental papillae, foul smell and gingival bleeding.

Treatment: Supportive care, pain control, use of oxidizing mouthwash, followed by periodontal surgery.

Q. 6. Write a short note on *C. diphtheriae*. (TNMGR, April 1998)

Ans. The bacillus is a slender rod with a tendency to clubbing; gram-positive; pleomorphic; nonsporing; noncapsulated; nonmotile; often show septa. Stained with **Loeffler's methylene blue**, the granules take up a bluish purple color and hence called metachromatic granules. They are also called **volutin or Babes Ernst granules**. They are often situated at the poles of the bacilli and are called polar bodies. Special stains, such as **Albert's**, **Neisser's** and **Ponders** have been devised for demonstrating the granules clearly. The bacilli are arranged in a characteristic fashion in smears (**Chinese letter or cuneiform arrangement**).

Cultural characteristics: The usual media for cultivation are Loeffler's serum slope and tellurite blood agar, McLeod's media and Hoyle's media. The

optimum temperature for growth is 37°C. The optimum pH 7.2. It is an aerobe and a facultative anaerobe. Colonies are at first small, circular white opaque discs but enlarge on continued incubation and may acquire a distinct yellow tint. Based on morphology on tellurite agar, bacilli are:

- i. *Gravis*: Daisy head colony.
- ii. *Intermedius*: Frog's egg colony.
- iii. *Mitis*: Poached egg colony.

Toxin: Diphtheria toxin is a protein and is extremely potent. The toxigenicity of the diphtheria bacillus depends on the presence in it of corynephages (tox+), which act as the genetic determinant controlling toxin production. Nontoxigenic strains may be rendered toxigenic by infecting them with *beta phage* or some other toxlarger phage. This is known as lysogenic or phage conversion.

Resistance: Cultures may remain viable for one or more weeks at 25-30°C. It is readily destroyed by heat in 10 minutes at 58°C and in a minute at 100°C. It is more resistant to the action of light, desiccation and freezing. It is susceptible to penicillin, erythromycin and broad spectrum antibiotics.

Antigenic structure: Diphtheria bacilli are antigenically heterogeneous. By agglutination, *gravis* strains have been classified into 13 types, *intermedius* into 4 types and *mitis* into 40 types.

Q. 7. Write a short note on diphtheria.

(TNMGR, April 2000)

Ans. Diphtheria, the name is derived from the tough, leathery pseudomembrane formed in the disease (diphtheros: leather). The diphtheria bacillus (*Corynebacterium diphtheriae*) is also known as the Klebs-Loeffler bacillus (KLB). The incubation period in diphtheria is commonly 3-4 days. The site of infection may be: Faucial; laryngeal; nasal; otitic; conjunctival; genital-vulval, vaginal or prepucial and cutaneous. According to the clinical severity, diphtheria may be classified as:

1. **Malignant or hypertoxic:** There is severe toxemia with marked adenitis (bull-neck). Death is due to circulatory failure.
2. **Septic:** Leads to ulceration, cellulitis and gangrene around the pseudomembrane.
3. **Hemorrhagic:** Characterized by bleeding from the edge of the membrane, epistaxis, conjunctival hemorrhage, purpura and bleeding tendency.

Complication

1. Asphyxia
2. Acute circulatory failure

3. Post-diphtheritic paralysis

4. Septic

Diphtheria is a toxemia. The bacilli remain confined to the site of entry, where they multiply and form the toxin. The toxin causes local necrotic changes and the resulting fibrinous exudate, together with the disintegrating epithelial cells, leukocytes, erythrocyte and bacteria, constitute the characteristic **pseudomembrane**. The mechanical complications of diphtheria are due to the membrane, while the systemic effects are due to the toxin.

Laboratory Diagnosis

1. **Smear** examination of the swab.
2. **Culture** of the swab on Loeffler's serum slope, Telurite blood agar and blood agar.

In vivo tests

1. Subcutaneous test
2. Intracutaneous test

In vitro test

1. Elek's gel precipitation test
2. Tissue culture test

Prophylaxis: Three methods of immunization are available:

- **Active immunization:** Diphtheria toxoid is given in children as a trivalent preparation containing tetanus toxoid and pertussis vaccine also, as the DTP, DPT or triple vaccine.
- **Passive immunization:** This is an emergency measure, 500-1000 units of antitoxin (antidiphtheritic serum—ADS).
- **Combined immunization:** It consists of administration of the first dose of adsorbed toxoid on one arm, while ADS is given on the other arm, to be continued by the full course of active immunization.

Treatment: Specific treatment of diphtheria consists of antitoxic and antibiotic therapy. Antitoxins (20,000-100,000 U) should be given immediately when a case is suspected as diphtheria. *C. diphtheriae* is sensitive to penicillin and can be cleared from the throat within a few days by penicillin treatment. Erythromycin is more active than penicillin in the treatment of carriers.

Q. 8. Write a short note on pathogenesis of tetanus.

(TNMGR, April 2003)

Ans. *Clostridium tetani* has a little invasive power. Germination and toxin production occur only if favorable conditions exist, such as reduced O-R potential, devitalized tissues, foreign bodies or concurrent infection. The toxin produced locally is absorbed by

the motor nerve ending and transported to the central nervous system intraxonally. The toxin is specifically and avidly fixed by gangliosides of the grey matter of the nervous tissue. Tetanospasmin toxin specifically blocks synaptic inhibition in the spinal cord. The abolition of spinal inhibition causes uncontrolled spread of impulses initiated anywhere in the CNS. The results are muscle rigidity and spasms due to the simultaneous contraction of agonist and antagonist in the absence of reciprocal inhibition. The toxicity of tetanospasmin is influenced by the route by which it is administered. Given orally it is destroyed by the digestive enzymes. When the toxin is inoculated intramuscularly in one of the hind limbs tonic spasms of the muscles of the inoculated limb appear first. This is known as *local tetanus* and is due to the toxin acting on the segment of the spinal cord containing the motor, neurons of the nerve supplying the inoculated area. Subsequent spread of the toxin up the spinal cord causes 'ascending tetanus'. If the toxin is injected intravenously, spasticity develops first in the muscles of the head and neck and the spreads downwards (descending tetanus). This type resemble the naturally occurring tetanus in human beings.

Q. 9. Write a short note on tetanus and its prophylaxis.
(TNMGR, Oct. 2000)

Ans. Tetanus is characterized by tonic muscular spasms usually commencing at the site of infection and becoming generalized, involving the whole of the somatic muscular system.

Causes

1. Injury, especially puncture wound
2. Surgical operations
3. Local suppuration
4. Septic abortion
5. Unsterile injections

The incubation period is variable from two days to several weeks, but is commonly 6–12 days. The incubation period is of prognostic significance, the prognosis being grave when it is short. Fatality rate varies from 15–50%.

Laboratory diagnosis: The diagnosis is clinical. Demonstration of *Clostridium tetani* by microscopy, culture or by animal inoculation.

Prophylaxis: The available methods of prophylaxis are:

1. **Surgical prophylaxis:** Removal of foreign bodies, necrotic tissue and blood clots, to prevent an anaerobic environment favorable for the tetanus bacillus.

2. **Antibiotics prophylaxis:** Antibiotic prophylaxis aims at destroying or inhibiting tetanus bacilli and pyogenic bacteria in wounds so that the production of toxins prevented.
3. **Immunization:** Passive, active or combined—passive immunization is by injection of anti-tetanus serum (1500 IU, SC/IM) soon after receiving any tetanus prone injury. Active immunization is most effective method of prophylaxis. This is achieved by spaced injections of formol toxoid. The tetanus toxoid is given either alone or along with the diphtheria toxoid and the pertussis vaccine as the triple vaccine.

Combined immunization consists of administering to a non-immune person exposed to the risk of tetanus. Tetanus immune globulin (TIG) injection at one site, along with the first dose of toxoid at the contralateral site, followed by the second and third doses of toxoid at monthly intervals.

Q. 10. Write a short note on toxins produced by staphylococci.
(TNMGR, April 2000)

Ans.

a. Cytolytic toxins

1. **Alpha hemolysin:** It is a protein inactivated at 70°C, but reactivated paradoxically at 100°C. Alpha toxin is less active against human red cells. It is also leucocidal, cytotoxic, dermonecrotic, neurotoxic and lethal. It is toxic to macrophages, lysosomes, muscle tissues, renal cortex and the circulatory system.
2. **Beta hemolysin:** It is a sphingomyelinase, hemolytic for sheep cells, but not for human. It exhibits a "hot-cold phenomenon".
3. **Gamma hemolysin:** Composed of two separate proteins both of which are necessary for hemolytic activity.
4. **Delta hemolysin:** It has a detergent-like effect on cell membranes of erythrocytes, leucocytes, macrophages and platelets.
5. **Leucocidin (Panton-valentine toxin):** A two component toxin (S and F). Such bi-component membrane active toxins as the staphylococcal leucocidin and gamma lysin have been grouped as synergohymenotropic toxins.
- b. Enterotoxin:** This toxin is responsible for the manifestations of staphylococcal food poisoning—nausea, vomiting and diarrhea 2–6 hours. The toxin is relatively heat stable, resisting 100°C for 10–40 minutes. The toxin is believed to act directly on the autonomic nervous system to cause the illness.
- c. Toxic shock syndrome toxin (TSST)** is a potentially fatal multisystem disease presenting with fever,

hypotension, myalgia, vomiting, diarrhea, mucosal hyperemia and erythematous rash.

- d. **Exfoliative (epidermolytic) toxin:** This toxin is responsible for the 'staphylococcal scalded skin syndrome (SSSS)—exfoliative skin diseases in which the outer layer of epidermis gets separated from the underlying tissues. The severe form of SSSS is known as Ritter's disease in the newborn and toxic epidermal necrolysis (TEN) in older patients. Milder forms are pemphigus neonatorum and bullous impetigo.

Q. 11. Write a short note on toxins of streptococci.

(TNMGR, April 2003)

Ans.

1. **Hemolysin:** Streptococci produce two hemolysins, streptolysin 'O' and 'S'. Streptolysin O is so-called because it is oxygen labile. On blood agar, streptolysin O activity is seen only in pour plates and not in surface cultures. It is cardiotoxic, leukotoxic. Streptolysin 'O' is antigenic and anti-streptolysin 'O' appears in sera following streptococcal infection. Estimation of this antibody (ASO titer) is a standard serological procedure for the retrospective diagnosis of infection with *Str. pyogenes*. Streptolysin S is an oxygen stable hemolysin and so is responsible for the hemolysis seen around streptococcal colonies on the surface of blood agar plates. It is called streptolysin S since it is soluble in serum.
2. **Pyrogenic exotoxin (erythrogenic, dick, scarlatinal toxin):** The primary effect of the toxin is induction of fever and so it was renamed streptococcal pyrogenic exotoxin (SPE). Three types of SPE have been identified A, B and C.
3. **Streptokinase (fibrinolysin):** This toxin promotes the lysis of human fibrin clots by activating a plasma precursor (plasminogen). Fibrinolysin appears to play a biological role in streptococcal infections by breaking down the fibrin barrier around the lesions and facilitating the spread of infection.
4. **Deoxyribonucleases (streptodornase, DNAase):** These cause depolymerization of DNA.
5. **Nicotinamide adenine dinucleotidase (NADase, formerly diphosphopyridine nucleotidase, DPNase):** This acts on the coenzyme NAD and liberates nicotinamide from the molecule. It is believed to be leukotoxic.
6. **Hyaluronidase:** This enzyme breaks down the hyaluronic acid of the tissues. This favors the spread of infection along the intercellular spaces.
7. **Serum opacity factor:** Some M types of *Str. pyogenes* produce a lipoproteinase which produces opacity

when applied to agar gel containing horse or swine serum. This is known as serum opacity factor (SOP).

Q. 12. Write a short note on Gram's stain.

(TNMGR, Oct. 2011, 2013)

Ans. It was developed by Danish bacteriologist, Christian Gram in 1884.

Principle: It is based on the principle that some bacteria are capable of retaining crystal violet stain within them inspite the action of decolorizing agent (gram-positive bacteria) whereas some fail to do so (gram-negative bacteria).

Procedure

1. The fixed smear is covered with crystal violet solution and kept as such for 30–60 seconds.
2. By holding the slide at downward angle the stain is poured off. Iodine solution is poured over the smear to get rid of remaining stain and smeared is covered with fresh iodine solution for 60 seconds.
3. Iodine is washed with ethyl alcohol by simultaneous tilting the slide from side to side till color ceases to come out of preparation (10–20 seconds).
4. The smear is washed with water and stained with counter stain (safranin or neutral red) for 20–30 seconds. The slide is dried for examination.

Control: On the same slide, smears should be prepared from *Staph. aureus* (gram-positive), *Escherichia coli* (gram-negative) to act as control.

Characteristics seen in gram stained smear

1. Shape
2. Arrangement
3. Stain reaction
4. Quantity
5. Special character
6. Additional structures

Structures not seen on the gram stained smear

1. Flagella
2. Fimbria
3. Nuclei
4. Capsules

Q. 13. Write a short note on gram-negative bacterial cell wall.

(TNMGR, Oct. 2003)

Ans. The cell wall accounts for shape of the bacterial cell and provides the rigidity and ductility. The cell wall cannot be seen by light microscopy and does not stain with simple stains. It may be demonstrated by plasmolysis. When placed in a hypertonic solution, cytoplasm loses water by osmosis and shrinks while

the cell wall retains its original shape and size (bacterial ghost). The cell wall may also be demonstrated by microdissection, reaction with specific antibody, mechanical rupture of the cell, differential staining procedures or by electron microscopy. Bacterial cell walls are about 10–25 nm thick and account for about 20–30% of the dry weight of the cells. Chemically the cell wall is composed of mucopeptide (peptidoglycan or murein) scaffolding formed by N-acetyl glucosamine and N-acetyl muramic acid molecules alternating in chains, cross-linked by peptide chains. The interstices of this scaffolding contain other chemicals, varying in the different species. In general, the walls of the gram-positive bacteria have simpler chemical nature than those of gram-negative bacteria. The cell wall carries bacterial antigens that are important in virulence and immunity. The lipopolysaccharides (LPS) present on the cell walls of gram-negative bacteria account for their endotoxic activity and O antigen specificity (formerly known as the Boivin antigen). The LPS consists of three regions. **Region I** is the polysaccharide portion determining the O antigen specificity. **Region II** is the core polysaccharide. **Region III** is the glycolipid portion (lipid A) and is responsible for the endotoxic activities—pyrogenicity, lethal effect, tissue necrosis, anti-complementary activity, B cell mitogenicity, immunoadjuvant property and anti-tumor activity. The outermost layer of gram-negative bacterial cell wall is called the outer membrane, which contains various proteins known as **outer membrane proteins** (OMP). Cell wall synthesis may be inhibited by many factors, like lysozyme splits the linkages in the cell wall.

Q.14. Write a short note on *Mycobacterium tuberculosis*.

Ans. *M. tuberculosis* is a straight, gram-positive, acid fast bacillus. It is an obligate aerobe. The most widely solid media employed Lowenstein-Jensen medium without starch. Other media include Dorsat, Tarshis, Loeffler and Pawlowsky. On solid media it forms dry, rough, raised irregular colonies with a wrinkled surface. They are creamy white, becoming yellowish or buff-colored on further incubation. They are not heat resistant, being killed at 60°C in 15–20 minutes. They are relatively resistant to chemical disinfectant. Test used to identify are niacin test, aryl sulphatase test, neutral red test, catalase-peroxidase test, amidase test, nitrate reduction test. The mode of infection is by direct inhalation of aerosolized bacilli contained in droplet nuclei of expectorated sputum.

Q. 15. Write a short note on nosocomial infections.

(TNMGR, Oct. 2011)

Ans. It is defined as infection developing in a patient after admission to the hospital, which was neither present nor in its incubation period when the subject entered the hospital.

Factors Influencing Nosocomial Infection

1. The hospital environment is heavily laden by variety of organism.
2. Hospital microbial flora is generally multidrug resistant due to injudicious use of antibiotics.
3. Patients with pre-existing disease are more susceptible.
4. Diagnostic or therapeutic interventions may introduce the infection.
5. Blood and blood products may also transmit the infection.

Microorganism causing nosocomial infections: 60% cases are caused by aerobic gram-negative rods, 30% by gram-positive cocci, remaining 10% by viruses and fungi.

Nosocomial Infections

1. Urinary tract infection
2. Respiratory infection
3. Wound and skin infections
4. Burn infections
5. Gastrointestinal infections
6. Eye infections
7. *Miscellaneous:* Hepatitis B virus, HIV

Routes of Transmission

1. *Contact spread:* Direct or indirect
2. Airborne spread
3. Oral route
4. Parenteral route
5. Self infection

Prevention

1. The provisions of sterile instruments, dressings, surgical gloves, face masks, theatre clothing and fluids.
2. Thorough handwashing after any procedure.
3. Preoperative disinfection of the patient's skin.
4. Use of antiseptics for irrigation of the wound site.
5. Rational antibiotic prophylaxis.
6. Proper investigation of nosocomial infection and the treatment of the patients and carriers.

Q. 16. Write a short note on common anaerobic infections. (TNMGR, March 2007)

Ans. Anaerobic infections are usually endogenous and are caused by tissue invasion by bacteria normally present on respective body surfaces. These are typically polymicrobial.

Precipitating factors are trauma, tissue necrosis, impaired circulation, hematoma formation or presence of foreign body.

Anaerobic infections as per site

1. **CNS:** Brain abscess.
2. **Ear nose throat:** Chronic sinusitis, otitis media, orbital cellulitis.
3. **Mouth and jaw:** Ulcerative gingivitis, dental abscess, cellulitis, abscess and sinus of jaw.
4. **Respiratory:** Aspiration pneumonia, lung abscess, empyema.
5. **Abdominal:** Hepatic abscess, appendicitis, peritonitis, wound infection after colorectal surgery.
6. **Female genitalia:** Wound infection following genital surgery, tubo-varian abscess, and septic abortion.
7. **Skin and soft tissue:** Infected sebaceous cyst, axillary abscess, cellulitis, diabetic ulcer, gangrene.

Clinical Features

1. Production of foul or putrid odor
2. Pronounced cellulitis
3. Toxemia
4. Fever

Laboratory Diagnosis

1. **Specimen collection and transport:** By using tissue biopsy of aspiration. Swabs are transferred in Stuart's transport medium.
2. Direct microscopy.
3. **Culture:** Freshly prepared blood agar with neomycin, yeast extract, hemin and vitamin K, Gas Pak system, cooked meat broth, thioglycollate broth.
4. **Identification:** Colony morphology and pigmentation and fluorescence help in identification of anaerobes.
5. Antibiotic sensitivity tests. By disc diffusion or dilution method.

Treatment: Surgical drainage along with antimicrobial therapy (clindamycin and metronidazole, penicillin G).

4. VIROLOGY

Q. 1. Write a short note on viral inclusion bodies.

(TNMGR, Nov. 2001)

Ans. Inclusion bodies are structures with distinct size, shape, location and staining properties that can be demonstrated in virus infected cells under the light microscope. These are the most characteristic histological feature in virus infected cells. They may be situated in:

- i. **Cytoplasm:** Poxvirus
- ii. **Nucleus:** Herpesvirus
- iii. **Both:** Measles virus

They are generally acidophilic and can be seen as pink structures when stained with Giemsa or eosin methylene blue stains. Some viruses (e.g. adenovirus) form basophilic inclusions. Demonstration of inclusion bodies helps in the diagnosis of some viral infections.

1. **Negri bodies:** Intra-cytoplasmic eosinophilic inclusions in the brain cells help in diagnosis of rabies.
2. **Guarnieri bodies:** Smaller multiple inclusions seen in vaccinia infected cells.
3. **Bollinger bodies:** Large inclusions seen in fowl pox.
4. **Molluscum bodies:** Very large inclusions (20–30 μ) seen in molluscum contagiosum.
5. **Cowdry type A (intranuclear):** Variable size and granular appearance seen in herpesvirus, yellow fever virus.
6. **Cowdry type B (intranuclear):** More circumscribed and often multiple seen in adenovirus, poliovirus.

Q. 2. Write about viral infections of the oral cavity.

(MAHE, Dec. 1996; TNMGR, Oct. 1999)

Ans.

a. Herpes simplex infections

1. Herpes gingivostomatitis
2. Herpes labialis

b. Herpes-zoster infection

1. Chickenpox
2. Herpes zoster

c. Coxsackie virus infection

1. Herpangina
2. Hand, foot and mouth disease
3. Acute lymphonodular pharyngitis

d. Cytomegalovirus infection: Foot and mouth disease.

e. Human papilloma virus infection

1. Squamous papilloma.
2. Verruca vulgaris.
3. Condyloma acuminatum.
4. Molluscum contagiosum.

f. Epstein-Barr virus infection: Infectious mononucleosis.

g. Human immunodeficiency virus: AIDS.

Q. 3. Write a short note on herpes simplex virus.

(TNMGR, April 1995, 2013)

Ans. The herpes simplex virus (HSV) occurs naturally only in humans. There are two type of the herpes simplex virus.

1. HSV type 1 (human herpesvirus type 1 or HHV type 1):

Usually isolated from lesions in and around the mouth and is transmitted by direct contact or droplet spread.

2. HSV type 2 (HHV type 2): Responsible for the majority of genital herpes infections, transmitted venereally.

Primary infection is usually acquired in early childhood. Humans are the only natural hosts and the sources of infection are saliva, skin lesions or respiratory secretions. Asymptomatic carriers form the more important source of infection. The virus enters through defects in the skin or mucous membranes and multiplies locally with cell-to-cell spread. The virus enters cutaneous nerve fibers and is transported intra-axonally to the ganglia where it replicates. The virus remains latent in the ganglia, to be reactivated, to cause recurrent oral and genital ulcers.

The typical herpes lesions are thin walled, umbilicated vesicles, the roof of which breaks down leaving tiny superficial ulcers. They heal without scarring. Gingivostomatitis and pharyngitis are the most frequent conditions in primary infection and recurrent herpes labialis in recurrent infection.

Acute keratoconjunctivitis may occur by itself or by extension from facial herpes. HSV has been implicated in the etiology of Bell's palsy. HSV esophagitis may cause dysphagia substernal pain and weight loss. It may involve the respiratory tract causing laryngo-bronchitis and pneumonitis. HSV is an uncommon cause of hepatitis. Erythema multiforme may be seen in association with HSV infection. Disseminated HSV infection may occur in patients with immunodeficiency, malnutrition or burns.

Laboratory diagnosis: The diagnosis of herpesvirus infection may be made by microscopy, antigen or DNA detection, virus isolation or serology.

The Tzanck smear is a rapid, fairly sensitive and in expensive diagnostic method. The herpesvirus antigen may be demonstrated in smears by the fluorescent antibody technique. The fluorescent antibody test on brain biopsy specimens provides reliable and speedy diagnosis in encephalitis. PCR based DNA detection has replaced brain biopsy.

Virus isolation by tissue culture can be used.

Serological methods are useful in the diagnosis of primary infections, as there is rise in antibody titers.

Treatment: Idoxuridine used topically in eye and skin infection. Oral and topical use of acyclovir may help in less serious conditions. Valaciclovir and famciclovir are more effective oral agents.

Q. 4. Write about prophylaxis for the control of hepatitis B virus infection.

(TNMGR, Aug. 2004)

Q. Write a short note on hepatitis B vaccine.

(TNMGR, April 2001)

Ans. General prophylaxis consists of avoiding risky practices like promiscuous sex, injectable drug abuse and direct or indirect contact with blood, semen or other body fluids of patients and carriers. Only certain method appears to be universal immunization. Both passive and active methods of immunization are available.

Passive immunization: Hyperimmune hepatitis B immune globulin (HBIG) prepared from human with high titer anti-HBs, administered IM in a dose of 300–500 IU soon after exposure. It may not prevent infection, but protects against illness and the carrier state.

Active immunization is more effective. The currently preferred vaccine is genetically engineered by cloning the S gene of HBV in bakers' yeast. It consists of nonglycosylated HBsAg particles alone. It is given with alum adjuvant, IM into the deltoid, or in infants into the anterolateral aspect of the thigh. Three doses given at 0, 1 and 6 months constitute the full course. A special vaccine containing all antigenic components of HBsAg (Pre-S1, Pre-S2 and S) has been developed. Booster doses are needed only for those at high risk.

Combined: For babies born to carrier mothers, a single injection of 0.5 ml of HBIG given IM immediately after birth is followed by the full course of vaccine at a different anatomical site, the first dose being given within 12 hours of birth.

Q. 5. Write about modes of transmission of hepatitis B infection.

(TNMGR, March 2007)

Ans. HBV is a bloodborne virus and the infection is transmitted by parenteral, sexual and perinatal modes. Blood of the carriers and the patients is the most important source of infection. The virus may also be present in other body fluids such as saliva, breast milk, semen, vaginal secretions, urine, bile and feces.

1. Transfusion of carrier blood: Most widely known mode of infection. Other includes shared syringes, needles, razors, acupuncture, tattooing.

2. Congenital or vertical transmission: Quite common for carrier mothers the risk is high if the mother is HBeAg positive.

3. Sexual transmission: More important particularly in promiscuous homosexual.

Q. 6. Write a short note on human immunodeficiency virus (HIV). (TNMGR, March 008; Sept. 2009)

Ans. HIV virus belongs to lentivirus subgroup of family Retroviridae.

Structure: HIV is a spherical enveloped virus about 90–120 nm in size. The nucleocapsid has an outer icosahedral shell and an inner cone-shaped core, enclosing the ribonucleoproteins. The genome is composed of two identical single-stranded, positive sense RNA copies along with reverse transcriptase enzyme (Fig. 5.1).

Viral genes and antigens: The genome of HIV contains three structural genes—*gag*, *pol*, *env*. The product of these genes act as antigens.

a. Genes coding for structural proteins

1. *gag* gene: Determine the core and shell of virus. It is expressed as precursor protein p55 which further cleaves into p15, p18, p24.
2. *pol* gene: Codes for polymerase reverse transcriptase and other enzymes. It further cleaves into p31, p51, p66.
3. *env* gene: Determine the synthesis of envelope glycoprotein gp160, which further cleaves into gp120—forms surface spikes, gp41—transmembrane anchoring protein.

b. Nonstructural and regulatory genes: *tat*; *nef*; *rev*; *vif*; *vpu*; *vpx*; *vpr*; LTR.

HIV is highly mutable virus with frequent antigenic variations. It is thermolabile, being inactivated in 10 minutes at 60°C and in seconds at 100°C. at room temperature, in dried blood it may survive for up to 7 days.

HIV is inactivated in 10 minutes by treatment with 50% ethanol, 35% isopropanol, 0.5% lysol, 0.3% hydrogen peroxide, and 10% household bleach. The standard recommendation is hypochlorite solution (0.5%). For contaminated instruments 2% glutaraldehyde is useful.

Q. 7. Write the oral manifestations of AIDS, transmission and prevention. (TNMGR, April 1995; UHSR, April 2009)

Ans. Oral manifestations of AIDS

Group 1: Lesions strongly associated with HIV infection

1. *Candidiasis*: Pseudomembranous, erythematous, angular cheilitis.
2. *Periodontal diseases*: Linear gingival erythema, necrotizing ulcerative gingivitis/periodontitis.
3. Non-Hodgkin's lymphoma
4. Hairy leukoplakia
5. Kaposi's sarcoma

Group 2: Lesions less commonly associated with HIV infection.

1. *Bacterial infections*: *Mycobacterium avium intracellulare*, *Mycobacterium tuberculosis*.
2. Melanotic hyperpigmentation
3. Necrotizing ulcerative stomatitis
4. *Salivary gland disease*: Hyposalivation, swelling of gland
5. Thrombocytopenic purpura
6. Viral infections: HSV, HPV, and VZV
7. Ulceration NOS (not otherwise specified)

Group 3: Lesions seen in HIV infection

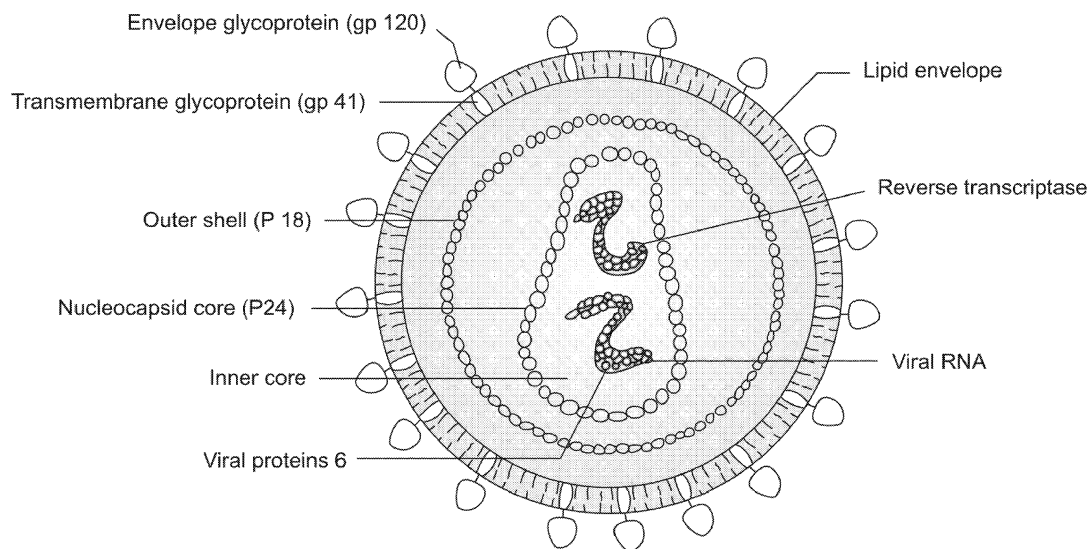


Fig. 5.1: Structure of human immunodeficiency virus (HIV)

1. *Bacterial infections*: Actinomyces, *E. coli*, Klebsiella infection.
2. *Fungal infection other than candidiasis*: Cryptococcosis, histoplasmosis, aspergillosis.
3. Recurrent aphthous stomatitis.
4. *Drug reactions*: Ulcerative lesion, EM, lichenoid reaction, toxic epidermolysis.
5. Bacillary epithelioid angiomatosis.
6. *Neurological disturbances*: Trigeminal neuralgia and facial palsy.
7. *Viral infections*: Molluscum contagiosum and CMV infection.

Transmission of HIV: Three main modes:

1. Through sex
2. Through blood and body fluids
3. Through mother to child transmission

Prevention: Universal precautions

1. Wash hands after patient contact.
2. Wash hands immediately if hands contaminated with body fluids.
3. Wear gloves when contamination of hands with body substances anticipated.
4. Protective eyewear and mask should be worn when splashing with body substances anticipated.
5. Take precautions to prevent injuries during procedures.
6. Needle should not be recapped.
7. Needles should not be purposely bent or broken by hand.
8. After use the sharp items should be placed in a puncture resistant container.
9. Personnel with any open skin wound should refrain from direct patient care and handling of equipment.
10. All needle stick injuries should be reported to the infection control officer.
11. Handle and dispose of sharps safely.
12. Clean and disinfect blood/body substances spills with appropriate agents.
13. Adhere to disinfection and sterilization standards.
14. Consider all the waste soiled with blood/body fluids as contaminated and dispose the same according to the relevant standards.
15. Vaccinate all clinical and laboratory workers against hepatitis B.
16. Adopt measures like double gloving, changing surgical techniques to avoid exposure prone procedures, use of needleless systems and other safe devices.

5. MYCOLOGY

Q. 1. Write a short note on oral thrush.

(TNMGR, Aug. 2004)

Ans. Oral thrush or pseudomembranous candidiasis is the most prevalent opportunistic infection affecting the oral mucosa, caused by yeast-like fungus *Candida albicans* and occasionally by other *Candida* species. Oral thrush is common in bottle fed infants and the aged and debilitated. Clinically, creamy white patches appear on the mucosa that leaves a red oozing surface on removal. Local predisposing factors include denture wearing, smoking, steroid inhalation, and hyperkeratosis. General predisposing factors include immunosuppression, chemotherapy, endocrinal disorders and anemia. Diagnosis can be established by microscopy and culture on Sabouraud agar.

Management: Removal of the predisposing cause. All the *Candida* strains are sensitive to nystatin and clotrimazole. Amphotericin B, 5-fluorocytosine and clotrimazole may be used for disseminated candidiasis.

Q. 2. Write a short note on *Candida albicans*.

(TNMGR, Nov. 1995)

Ans. *Candida albicans* the causative organism of the opportunistic infection candidiasis. It is an ovoid or spherical budding cell which produces pseudomycelia both in culture and in tissues. *Candida* species are normal inhabitants of the skin and mucosa.

On culture media, the colonies are creamy white, smooth and with a yeast odor. It also forms chlamydospores on corn meal agar cultures at 20°C. A rapid method of identifying *C. albicans* is based on its ability to form germ tubes within two hours when incubated in human serum at 37°C (Reynolds-Braude phenomenon).

Q. 3. Write a short note on media used in mycology.

(TNMGR, March 2007)

Ans. The commonest culture media used in mycology are:

1. Sabouraud's glucose agar
2. Czapek-Dox medium
3. Corn meal agar

The addition of antibiotics prevents bacterial contamination. Cultures are routinely incubated in parallel at room temperature (22°C) for weeks and at 37°C for days. Identification is based on the morphology of fungus and its colony. Growth characteristics useful for identification are rapidity of growth, color, and morphology of the colony.

6. STERILIZATION AND INFECTION CONTROL

Q. 1. Define the terms sterilization and disinfection. Describe the mechanism of action and uses of various chemical disinfectants.

(TNMGR, April 2001; March 2008; BPUHS, May 2009; RGUHS, May 2011)

Ans. Sterilization is defined as the process by which an article, surface or medium is freed of all living micro-organisms either in the vegetative or spore state. Disinfection means the destruction or removal of all pathogenic organisms, or organisms capable of giving rise to infection.

A. Physical Agents

1. **Sunlight:** The action is primarily due to UV rays.
2. **Drying:** Drying has deleterious effect on many bacteria.
3. **Dry heat:** Most reliable method of sterilization.
 - i. **Flaming:** Inoculating wire, tip of forceps, spatulas in flame, till they become red hot.
 - ii. **Incineration:** For contaminated clothes, pathological materials, etc.
 - iii. **Hot air oven:** Most widely used method of dry heating. Holding period of one hour on 160°C to sterilize glassware, forceps, scissors, scalpels, glass syringes, swabs, liquid paraffin, dusting powder.
4. **Moist heat sterilization**
 - i. **Pasteurization:** Milk is heated at either 63°C for 30 minutes (the holder method) or 72°C for 15–20 seconds (the flash process) followed by cooling quickly to 13°C or lower. Vaccine, serum or body fluids, Lowenstein-Jensen and Loeffler's serum are rendered sterile by this method.
 - ii. **Boiling:** The material should be immersed in the water and boiled for 10–30 minutes.
 - iii. **Steam under normal pressure:** Koch or Arnold steamer is used. This is based on Tyndallization or intermittent sterilization—exposure of culture media to 100°C for 20 minutes on three successive days.
 - iv. **Steam under pressure:** The principle of the autoclave or steam sterilizer is that water boils when its vapor pressure equals that of the surrounding atmosphere.
5. **Filtration:** With the help of candles, asbestos pads, and membranes.
6. **Radiation**
 - i. **Non-ionizing radiation:** Infrared and UV rays for sterilization of prepacked items such as syringes and catheters; entryways, operation theaters, and laboratories.

- ii. **Ionizing radiation:** X-rays, gamma rays, cosmic rays (cold sterilization) for plastics, syringes, swabs, catheters, etc.

7. Ultrasonic and sonic vibrations.

B. Chemical Agents

1. **Alcohols:** Ethyl alcohol and isopropyl alcohol are the most frequently used. They are used mainly as skin antiseptics and act by denaturing bacterial proteins. To be effective, they must be used at a concentration of 60–90% in water. Isopropyl alcohol is preferred as it is a better fat solvent, more bactericidal and less volatile. It is used for the disinfection of clinical thermometers. Methyl alcohol is effective against fungal spores and is used for treating cabinets and incubators affected by them.
2. **Aldehyde**

Formaldehyde: It is active against the amino group in the protein molecule. In aqueous solutions, it is bactericidal, sporicidal and lethal effect on viruses. It is used to preserve anatomical specimens. 10% formalin containing 0.5% sodium tetraborate is used to sterilize clean metal instruments. Formaldehyde gas is used for sterilizing instruments and heat sensitive catheters and for fumigating wards, sick rooms and laboratories. Under properly controlled conditions, clothing, bedding, furniture and books can be satisfactorily disinfected.

Glutaraldehyde: This has an action similar to formaldehyde. It is especially effective against tubercle bacilli, fungi and viruses. It is less toxic and irritant to the eyes and skin than formaldehyde. It can be safely used to treat corrugated rubber anesthetic tubes and face masks, plastic endotracheal tubes, metal instruments and polythene tubing.
3. **Dyes:** Dyes are used as skin and wound antiseptic, having bacteriostatic activity with low bactericidal activity.
 - i. **Aniline dyes:** Brilliant green, malachite green, crystal violet. More active against gram-positive organisms, used in the microbiology laboratory as selective agents in culture media. They react with the acid groups in the cell.
 - ii. **Acridine dyes:** Proflavine, acriflavine, euflavine and aminacrine. Most active against gram-positive organisms than against gram-negative. They impair the DNA complexes of the organisms and thus kill or destroy the reproductive capacity of the cell.
4. **Halogens:** Iodine in aqueous and alcoholic solution has been used widely as a skin disinfectant. It is actively bactericidal, with moderate action against

spores. Compounds of iodine with nonionic wetting or surface active agents known as **iodophores** are more active. Chlorine and its compounds are used as disinfectants for water supplies, swimming pools, food and dairy industries. Chlorine is used commonly as hypochlorite. The organic chloramines are used as antiseptics for dressing wounds.

5. **Phenols:** The lethal effect of phenols is due to their capacity to cause cell membrane damage releasing cell contents and causing lysis. Phenol (carbolic acid) is a powerful microbicidal substance. Lysol and cresol are active against a wide range of organisms. Hexachlorophene is potentially toxic and should be used with care. Chlorhexidine is a relatively nontoxic skin antiseptic.

6. **Gases** (TNMGR, April 2003)

- i. **Ethylene oxide:** At normal temperature and pressure is a highly penetrating gas with a sweet ethereal smell. Its action is due to its alkylating the amino, carboxyl, hydroxyl and sulphhydryl group in protein molecules. It is effective against all types of microorganisms including viruses and spores. It is specially used for sterilizing heart-lung machines respirators, sutures, dental equipment, books and clothing, glass, metal and paper surfaces, clothing, plastics, soil, some foods and tobacco.
 - ii. **Formaldehyde gas:** This is widely employed for fumigation of operation theatres and other rooms.
 - iii. **Betapropiolactone (BPL):** This is a condensation product of ketone and formaldehyde with a boiling point of 163°C. It is said to be more efficient for fumigating purposes than formaldehyde. For sterilization of biological products 0.2% BPL is used. It is capable of killing all microorganisms and is very active against viruses.
7. **Surface active agents:** Substances which alter energy relationship at interfaces, producing a reduction of surface or interfacial tension are referred to as surface active agents. They are classified into four main groups: Anionic, cationic, nonionic and amphoteric.
8. **Metallic salts:** Salts of silver, copper and mercury are use as disinfectant. They act by coagulation of proteins.

Q. 2. Write a short note on surface active agents.

(TNMGR, Oct. 2003)

Ans. Substances which alter energy relationship at interfaces, producing a reduction of surface or interfacial tension are referred to as surface active agents.

1. **Cationic compounds:** The most important anti-bacterial surface active agents. These act on the phosphate groups of the cell membrane and also enter the cell. The membrane loses its semi-

permeability and the cell proteins are denatured. The cationic compounds in the form of quaternary ammonium compounds are markedly bactericidal, being active against gram-positive organisms and to a lesser extent on gram-negative ones; they have no action on spores, tubercle bacilli and most viruses. The common compounds are: Acetyl trimethyl ammonium bromide (cetavlon or cetrimide) and benzalkonium chloride. These are most active at alkaline pH. Acid inactivates them. Organic matter reduces their action and anionic surface active agents render them inactive.

2. **Anionic compounds:** For example, common soap, have moderate action. Soaps prepared from saturated fatty acids (such as coconut oil) are more effective against gram-negative bacilli while those prepared from unsaturated fatty acids (oleic acid) have greater action against gram-positive and Neisseria group of organisms.
3. **Amphoteric or ampholytic compounds:** Also known as **Tego** compounds, are active against a wide range of gram-positive and gram-negative organisms and some viruses.

Q. 3. Write a short note on autoclave.

(TNMGR, April 1998; March 2007)

Ans. Principle: Water boils when its vapor pressure equals that of the surrounding atmosphere. Hence, when pressure inside a closed vessel increases, the temperature at which water boils also increases. Saturated steam has penetrative power. When steam comes into contact with a cooler surface it condenses to water and gives up its latent heat to that surface. The large reduction in volume sucks in more steam to the area and the process continue till the temperature of that surface is raised to that of the steam. The condensed water ensures moist conditions for killing the microbes present.

Sterilization by autoclave is carried out at temperatures between 108° and 147°C. By using the appropriate temperature and time variety of materials such as dressings, instruments, laboratory ware, media and pharmaceutical products can be sterilized. Aqueous solutions are sterilized between 108° and 126°C. Several types of steam sterilizers are in use:

1. Laboratory autoclaves
2. Hospital dressing sterilizers
3. Bowl and instrument sterilizers
4. Rapid cooling sterilizers

Parts of autoclave

- i. Vertical or horizontal cylinder of gun-metal or stainless steel

- ii. Supporting sheet iron case
- iii. Lid or door fastened by screw clamps and washer
- iv. Discharge tap for air and steam
- v. Pressure gauge
- vi. Safety valve

Working: Sufficient water is put in the cylinder, the material to be sterilized is placed on the tray, and the autoclave is heated. The lid is screwed tight with the discharge tap open. The safety valve is adjusted to the required pressure. The steam-air mixture is allowed to escape freely till all the air has been displaced. The steam pressure raises inside to a desired level, safety valve opens and the excess steam escapes. When the holding period is over, the heater is turned off and the autoclave allowed to cool till the pressure gauge indicates that the pressure inside is equal to the atmospheric pressure.

Q. 4. Write a short note on sterilization by chemical agents. (TNMGR, Oct. 2003; Sept. 2010)

Ans. Several chemical agents are used as antiseptics and disinfectants. An ideal antiseptic or disinfectant should

- 1. have a wide spectrum of activity and must be effective against all microorganisms
- 2. be active in the presence of organic matter
- 3. be effective in acid as well as alkaline media
- 4. gave speedy action

- 5. Have high penetrating power
- 6. Be stable
- 7. Be compatible with other antiseptics and disinfectants
- 8. Not corrode metals
- 9. Not cause local irritation or sensitization.
- 10. Not interfere with healing
- 11. Not be toxic if absorbed into circulation
- 12. Be cheap and easily available
- 13. Be safe and easy to use

The main modes of action are

- 1. Protein coagulation
- 2. Disruption of cell membrane
- 3. Removal of free sulfhydryl groups
- 4. *Substrate competition*
 - i. *Alcohols:* Ethyl alcohol and isopropyl alcohol methyl alcohol.
 - ii. *Aldehyde:* Formaldehyde, glutaraldehyde.
 - iii. *Dyes:* Aniline dyes and acridine dyes.
 - iv. *Halogens:* Iodine, chlorine and its compounds.
 - v. *Phenols:* Phenol (carbolic acid), lysol, cresol hexachlorophene and chlorhexidine.
 - vi. *Gases:* Ethylene oxide, formaldehyde gas, beta-propiolactone (BPL).
 - vii. Surface active agents.
 - viii. *Metallic salts:* Salts of silver, copper and mercury.

Q. 5. Write a short note on methods of sterilization of dental surgical instruments. (TNMGR, Oct. 1999)

Ans.

S. No.	Equipment	Suggested treatment
1.	Dental handpiece	Autoclave (used lubricant spray prior to autoclaving)
2.	Mouth mirrors, probes, tweezers, excavators, chisels, pluggers, carvers, matrix, bands and holders, cartridge syringes.	Autoclave (scrub clean first)
3.	Forceps, elevators, scalpel handles, retractors and other surgical instruments.	Autoclave (scrub clean first)
4.	Endodontic files and brooches	Autoclave (may be dipped in alcohol and flamed during treatment)
5.	Periodontal scalers and surgical instruments	Autoclave (scrub clean first)
6.	Air/water spray nozzles	Autoclave if possible or disinfect with clear phenolic or chlorhexidine in alcohol (removable tips advised)
7.	Dental burs (steel)	Disposable
8.	Tungsten carbide and diamond burs	Treat in ultrasonic bath, then autoclave
9.	Orthodontic bands and wires	Disposable (use clean and discard on removal)
10.	Orthodontic pliers	Autoclave or disinfect with clear phenolic or chlorhexidine in alcohol.
11.	Prosthetic trays (metal trays)	Autoclave
12.	Plastic trays	Disposable
13.	Tumblers	Disposable (plastic, paper cups), if glass/metal: Washing in hot water with detergent
14.	Gauzes, cotton wool, paper point	Autoclave after wrapping (do not pack tightly)
15.	Linen	Autoclave surgical drapes after wrapping otherwise freshly laundered linen is satisfactory

(Contd.)

(Contd.)

S. No.	Equipment	Suggested treatment
16.	Needles for syringe	Disposable (never reuse)
17.	Local anesthetic cartridges	Sterilized by manufacturer and disposable
18.	Impression compounds, saliva ejectors, sutures and needles	Disposable
19.	Suction tips	Autoclave
20.	Spatula and glass mixing slabs	Wash with hot water and detergent (if not infected). If contaminated with saliva, then autoclave spatula; disinfect slabs with hypochlorite
21.	Face masks for general anesthetic apparatus	Wipe with hypochlorite and wash in clean water before reuse
22.	Scrubbing brushes	Do not use routinely
23.	Surgery floors	Wash with detergent and dry, daily
24.	General working surfaces	Wash with detergent and dry, daily
25.	Bracket table	Wipe with chlorhexidine in alcohol or in 70% isopropyl alcohol in water, in between patients
26.	Lamps	Wipe of dust daily
27.	Cleaning equipment (bucket, mops, clothes, etc.)	Rinse and store dry

Q. 6. Write a short note on disposal of infectious waste. (TNMGR, Nov. 2001)

Ans. Chemical disinfection—contaminated materials like sputum or pus needs to be disinfected before being buried or autoclaved.

- 1. Deep burial:** Materials after chemical disinfection are put in deep trenches, covered with lime and filled with soil, safe method for sharps also.
- 2. Incineration:** It is safe method for large solid infectious waste like anatomical waste, amputated limbs, and animal carcasses.
- 3. Autoclaving:** Used in laboratories and clinics for disposal of infectious waste.
- 4. Microwave:** Useful method of sterilization of small volume waste at the point of generation.
- 5. Liquid waste:** Pathological, chemical and toxic liquid waste should be treated with disinfectants and neutralized before flushing into the sewer.

Q. 7. Write a short note on disposal of wastes in dental office. (UHSR, April 2013; TNMGR, April, 2015)

Ans.

a. Non-anatomical wastes (blood soaked materials): All biomedical wastes must be color-coded and marked with biohazard symbol. Biomedical wastes can only be transported by a company with proper certification. Non-dripping gauze and extracted teeth are not considered biomedical; however teeth with amalgam restorations cannot be placed in the incinerator for disposal.

Management: Use a yellow biomedical waste bag to collect the non-anatomical wastes and then double bag the waste, label the bag with a biohazard symbol. Never throw blood soaked materials into the regular garbage or into the compost waste and never place them in the sharps container.

b. Non-anatomical wastes: All sharps must be disposed using the appropriate guidelines.

Management: Collect sharps in a red or yellow puncture resistant container with a lid that cannot be removed. The sharps container should be properly labeled with biohazard symbol. Once container is full, the biomedical waste should be disposed by contacting a certified biomedical waste carrier. Do not fill over-full to prevent injury. Do not dispose the syringes and needles as it is. Always cut the needle with a needle cutter and dispose it otherwise the rag pickers are likely to pick up these syringes and needles and it gets recirculated into the main stream.

Needle disposal: The waste containers are designed for proper disposal of used needles. Containers are environmentally safe. When burned properly at a waste disposal facility, containers emit only carbon dioxide and water.

Elemental Mercury Waste

Management: Store unused elemental mercury in a tightly sealed, break resistant container and label those containers properly "Hazardous Waste". Contact a certified waste carrier for recycling or disposal.

Use a "mercury spill kit" if you have a spill of elemental mercury.

Scrap Amalgam

Management: Use a sponge type mercontainer to store the scrap amalgam. Empty amalgam capsules are non-hazardous and can be disposed in the garbage. Use an amalgam separator on the suction lines to remove over 95% of the contact amalgam prior to entering the sewer system. Use disposable suction traps dental units and change them weekly. Use gloves, mask, and glasses when cleaning the suction traps. Place the used

disposable trap into a properly labeled container for proper disposal. Once full, contact a certified waste carrier for recycling or disposal. Use a properly labelled container with mercury vapor suppressant such as fixer to submerge the amalgam particles. Manually remove large pieces of amalgam which are produced when removing old fillings and place them in a contact amalgam container. Consider using amalgam substitutes in cases where they are appropriate. Never dispose scrap amalgam in the garbage and never wash it down the drain. Do not place scrap amalgam in the sharps container and never rinse the traps and filters in the sink as amalgam particles will discharge into the sewer. Do not throw disposable traps that contain amalgam particles into the garbage. Do not place extracted teeth with amalgam fillings in the regular garbage. It should be disposed of in the "Scrap Amalgam" container to avoid incineration. Do not suction up unused particles of amalgam, instead place them in a mercury vapor suppressant container.

Used X-ray fixer solution: It is considered hazardous waste because of its high silver content. It can be managed with the help of reclamation facility/hazardous waste management firm. Use silver recovery units.

X-ray developer: It can be flushed down the drain.

Lead: An additional byproduct of traditional radiography is the lead shields contained in each film packet. Although the lead shields themselves are relatively small, the cumulative waste produced can be considerable. An added benefit of digital radiography is the reduction in lead waste production. Even at low levels of exposure, lead exerts adverse health effects on both children and adults. Reducing environmental lead contamination by dental practitioners is an inexpensive and easy task. The lead shields from film packets merely have to be collected and returned periodically to the manufacturer for recycling.

General office waste: Purchase of products with minimal packaging and use of reusable plastic containers (e.g. for cleaning and disinfecting solutions) can reduce general waste production. Products made from recycled or partly recycled materials can also be used (e.g. cotton or wool rolls, paper towels). Energy-efficient lighting and temperature regulation can limit office energy use. Single-spaced printing and use of both sides of pages can decrease the amount of paper used in the dental office.

Q. 8. Write in detail about infection control in dental clinics.

(BFUHS, Nov. 2002; TNMGR, March 2008; MUHS, May 2010; UHSR, April 2013)

Q. Write a short note on cross infection.

(TNMGR, Sept. 2007; UHSR, May 2012)

Ans. All procedures adopted to eliminate factor or factors identified to be responsible for causing infection/cross infection. **Cross infection** is spread of infection from one source to another, such as person to person, animal to person and animal to animal.

CDC have given guidelines for infection control in dental practice under universal or standard precautions, which is based on the concept that all blood and body fluids might be contaminated and should be treated as infectious because patients with bloodborne infections can be asymptomatic or unaware that they are infected.

Infection control procedures to be adopted by dental health care personnel (DHCP):

a. Environmental infection control: Act of rendering the environment free of contamination. In dental practice, a variety of environmental surfaces could become contaminated with patient material during treatment procedure. For example, light handles, switches, drawer knobs, etc. this can be cleaned by thorough cleaning and by using barrier protection. Floor, walls and sinks should be kept clean by simple cleaning with use of water and detergent.

b. Personal protection measures

1. **Immunization:** All the DHCPs should be vaccinated against HBV. A booster dose after 5 years of primary course is recommended.
2. **Protective clothing:** Full sleeve lab coat should be worn over the street clothing while treating patients.
3. **Hand hygiene (washing):** Handwashing should be done before and after treating the patient. Types of handwashing agents:
 - i. Routine handwash: Water and plain soap.
 - ii. Antiseptic handwash: Water and antimicrobial soap.
 - iii. Antiseptic hand rub: Alcohol based hand rub.
 - iv. Surgical antisepsis: Water and plain soap followed by alcohol based hand rub.
4. **Hand gloves and their correct use**
 - i. Before and after use of gloves, hands should be thoroughly washed and dried.
 - ii. Gloves for medical purpose are intended for single use.
 - iii. Correct size gloves should be worn.

5. *Mask, protective eyewear and face shield:*
 - i. Masks are important to prevent droplet infection.
 - ii. Surgical masks protect the wearer from micro-organism generated by water.
 - iii. Masks should be changed frequently, as they become wet easily.
 - iv. Majority of the surgical masks do not offer adequate protection against tuberculosis.
 - v. Eyewear/face shields provide protection against splashes of sprays of blood and body fluids.
6. *Avoidance of occupational injuries:* By following safe practices injuries and exposure to patients body fluids should be avoided.
7. *Health status of DHCP:* DHCP monitor their own status, work related illness.

Patient Procedures in Infection Control

1. A thorough and updated medical history, identifying any infective diseases should be recorded.
2. Patient should be encouraged to maintain proper oral hygiene.
3. Protective clothing should be used for the patient.
4. Rubber dam and suction should be used appropriately.
5. Use of preprocedural antimicrobial mouth rinses should be encouraged.

Role of sterilization: Sterilization and disinfection of patient care items:

- a. *Critical items:* Penetrates soft tissues, contact bone, and enters into blood. For example, surgical instrument, periodontal scalers, scalpel blades, surgical dental burs. They have the greatest risk of transmitting infection; therefore they should be sterilized by heat.
- b. *Semicritical items:* Contacts mucous membrane or non-intact skin. For example, mouth mirrors, amalgam condenser, reusable impression trays, dental hand pieces. They should be sterilized by heat.
- c. *Noncritical items:* Contact intact skin. For example, radiograph cone, BP cuff, facebow, pulse oximeter. They should be cleaned and if visibly soiled, should be disinfected with disinfectant.

Other Aspects of Infection Control

1. **Dental unit water lines:** Several microorganisms can colonize these water lines, majority of which are common heterotrophic water bacteria.
2. **Dental unit water quality:** Flushing waterline for 2–3 minutes first thing is recommended.
3. **Special considerations:** Semicritical equipment attached to waterline should be run to discharge air

or water for a minimum of 20–30 seconds after each patient.

4. **Handling of biopsy specimen:** Each specimen must be placed in a sturdy, leak proof container with a secure lid.
5. **Dental radiology:** Gloves must be worn while taking radiograph. After the exposure the film should be dried with gloved hands.
6. **Dental laboratory material:** Alginate and polymer impression material should be dipped in 1 in 10 solution of sodium hypochlorite for several seconds.
7. **Disposal of clinical waste material and sharps**
 - i. Discarded extracted teeth should be disposed in medical waste containers.
 - ii. Clinical waste should be carefully handled with gloved hands, placed and sealed in a leak proof container with bin liner.
 - iii. Contamination of outer surfaces of bin should be avoided.
 - iv. Appropriate biolabeling signs should be placed on the bags.
 - v. Sharps should be placed in a strong puncture proof container.
 - vi. Liquid waste may be carefully poured into the drain connected to sewer system.
8. **Management of blood spills:** Blood spills should be removed with wearing gloves and other protective wear. Visible organic material should be cleaned with absorbent material. Nonporous surfaces should be cleaned and decontaminated with disinfectant effective against HBV and HIV.

Q. 9. Write a note on hospital waste management.
(RGUHS, May 2011; TNMGR, Oct. 2011)

Ans. Biomedical waste is defined as any waste which is generated during the diagnosis, treatment or immunization of human beings in research activities pertaining to thereto or in production or testing of biological.

Categories of Biomedical Waste

Category	Waste category	Treatment and disposal
1.	Human anatomical waste	Incineration; deep burial
2.	Animal waste	Incineration; deep burial
3.	Microbiology and biotechnology waste	Autoclaving/microwaving/incineration
4.	Waste sharps	Disinfection (chemical treatment; autoclaving/microwaving) and mutilation/shredding

(Contd.)

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Category	Waste category	Treatment and disposal
5.	Discarded medicines and cytotoxic drugs	Incineration
6.	Solid waste (blood contaminated cotton, dressings, soiled plaster casts, linen, beddings)	Autoclaving/microwaving/incineration
7.	Solid waste (tubings, catheters, IV sets, etc.)	Disinfection (chemical treatment; autoclaving/microwaving) and mutilation/shredding
8.	Liquid waste	Disinfection by chemical treatment and discharge into drain
9.	Incineration ash	Disposal in municipal landfill
10.	Chemical used in disinfection	Disinfection by chemical treatment and discharge into drain for liquids and landfill for solids

Color Coding of Bags and Categories

Color coding bags	Waste categories
Yellow	1, 2, 3, 6
Red	3, 6, 7
Blue/white translucent	4, 7
Black	5, 9, 10

7. LABORATORY INVESTIGATIONS

Q. 1. Write a short note on immunofluorescein tests.
(RGUHS, May 2011)

Ans. The commonly used fluorescent dyes are fluorescein isothiocyanate and lissamine rhodamine. Immunofluorescence tests are of two types.

1. Direct Immunofluorescence Test

Principle: The specific antibodies tagged with fluorescent dye (labeled antibodies) are used for the detection of unknown antigen in a specimen. If antigen is present, it reacts with labeled antibodies and fluorescence can be observed under UV light of fluorescent microscope.

Uses

- It is commonly used for the detection of bacteria, viruses or other antigens in blood, CSF, urine, faces, tissues and other specimens.
- It is a sensitive method to diagnose rabies by detection of rabies virus antigens in brain smears.

Disadvantage of this method is that separate fluorescent conjugate have to be prepared against each antigen to be tested.

2. Indirect Immunofluorescence Test

It is used for detection of antibodies in serum or other body fluids.

Principle: A known antigen is fixed on a slide. The unknown antibody (serum) is applied to the slide. If antibody (globulin) is present in the serum, it attaches to the antigen on the slide. For detection of this, antigen antibody reaction, fluorescein in tagged antibody to human globulin is added. In positive test, fluorescence occurs under UV light.

It uses an antiglobulin fluorescent conjugate, to overcome the disadvantage of direct immunofluorescence. For example, fluorescent antibody test for the diagnosis of syphilis. Here a drop of test serum is placed on a smear of *T. pallidum* on a slide and after incubation, the slide is washed well to remove all free serum, leaving behind only antibody globulin, if present coated on the surface of the treponemes. The smear is then treated with a fluorescent labeled antiserum to human gammaglobulin. The fluorescent conjugate reacts with antibody globulin bound to the treponemes. After washing away all the unbound fluorescent conjugate, when the slide is examined under UV illumination, if the test is positive, the treponemes will be seen as bright objects against a dark background. If the serum does not have antitreponemal antibody, there will be no globulin coating on the fluorescent conjugates. A single antihuman globulin fluorescent conjugate can be employed for detecting human antibody to any antigen.

Q. 2. Write a short note on laboratory diagnosis of diphtheria.
(TNMGR, Nov. 1995)

Ans. Laboratory diagnosis consists of isolation of the diphtheria bacillus and demonstration of its toxicity. One or two swabs from the lesions are collected under vision, using a tongue depressor. Diphtheria bacilli may not always be demonstrable in smears from the lesion. Toxigenic diphtheria bacilli may be identified in smears by immunofluorescence. For culture the swab are inoculated on Loeffler's serum slope. Telurite blood agar and a plate of ordinary blood agar, the last for differentiating streptococcal or staphylococcal pharyngitis.

Virulence tests

- In vivo* tests
 - Subcutaneous test

2. Intracutaneous test
- b. *In vitro* tests
 1. Elek's gel precipitation test
 2. Tissue culture test

Q. 3. Write a short note on Widal test.

(TNMGR, March 2002)

Ans. This is a test for the measurement of H and O agglutinins for typhoid and paratyphoid bacilli in the patient's sera. Equal volumes (0.4 ml) of serial dilutions of the serum (from 1/10 to 1/640) and the H and O antigens are mixed in Dreyer's and Felix agglutination tubes, respectively, and incubated in a water bath at 37°C overnight. Control tubes containing the antigen and normal saline are set to check for auto-agglutination. The agglutination titers of the serum are read. H agglutination leads to the formation of loose, cotton woolly clumps, while O agglutination is seen as a disc like pattern at the bottom of the tube. The antigens used in the test are the H and O antigens of *S. typhi* and the H antigens of *S. paratyphi* A and B. The H agglutinable suspension is prepared by adding 0.1% formalin to a 24-hour broth culture or saline suspension of an agar culture. For preparing the O suspension, the bacillus is cultured on phenol agar (1:800) and the growth scraped off in a small volume of saline. It is mixed with 20 times its volume of absolute alcohol, heated at 40–50°C for 30 minutes, centrifuged and the deposit resuspended in saline to the appropriate density. The strain used usually is the *S. typhi* 901, 'O' and 'H' strains. Each batch of antigen should be compared with a standard. The results of the Widal test should be interpreted taking into account the following:

1. The agglutination titer will depend on the stage of the disease. Agglutinins usually appear by the end of the first week, so that blood taken earlier may give a negative result.
2. Demonstration of a rise in titer of antibodies, by testing two or more serum samples is more meaningful than a single test.
3. Agglutinins may be present on account of prior disease in apparent infection or immunization.
4. Persons who have had prior infection or immunization may develop an anamnestic response during an unrelated fever.
5. Bacterial suspensions used as antigens should be free from fimbria.
6. Cases treated early with chloramphenicol may show a poor agglutinin response.

Q. 4. Write about laboratory diagnosis of pulmonary tuberculosis.

(Bombay Uni., Oct. 1985; TNMGR, April 2001)

Ans. Laboratory diagnosis of tuberculosis may be established by demonstrating the bacillus in the lesion by microscopy, isolating it in culture or by transmitting the infection to experimental animal molecular methods. The specimen tested is the sputum. Sputum is best collected in the morning before any meal. Sputum sampling on three days increases chances of detection. Where sputum is not available laryngeal swabs or bronchial washings may be collected.

1. **Microscopy:** Sputum microscopy is the most reliable single method in diagnosis. Smears are dried, heat fixed and stained by Ziehl-Neelsen technique. Under the oil immersion objective, acid-fast bacilli are seen as bright red rods while the background is blue, yellow or green depending on the counter stain used. A negative report should not be given till at least 300 fields have been examined taking about 10 minutes. A positive report can be given only if two or more typical bacilli have been seen. When several smears are to be examined daily, it is more convenient to use fluorescent microscopy. Smears are stained with auramine phenol or auramine rhodamine fluorescent dyes and when examined under ultraviolet illumination, the bacilli will appear as bright rods against a dark background.
2. **Concentration methods:**
 - i. *Methods useful for microscopy:* Treatment with antiformin, sodium carbonate or hypochlorite, detergents like tergitol, flotation methods using hydrocarbons and the autoclave method.
 - ii. *Methods useful for culture and animal inoculation:* Petroff's method.
3. **Cultures:** Culture is a very sensitive diagnostic technique for tubercle bacilli. The concentrated material is inoculated onto at least two bottles of IUAT-LJ medium. Cultures are examined for growth after incubation at 37°C for four days and at least twice weekly thereafter. A negative report is given if no growth occurs after 8–12 weeks. Any growth seen is smeared and rested by ZN staining.
4. **Sensitivity tests**
 - i. Absolute concentration method
 - ii. Resistance ratio method
 - iii. Proportion method
5. **Animal inoculation:** The concentrated material is inoculated intramuscularly into the thigh of two healthy guinea pigs about 12 weeks old. The animals are weighed before inoculation and at intervals thereafter. Progressive loss of weight is an indication

of infection. Infected animals show a positive tuberculin skin reaction.

6. **Nucleic acid technology:** Polymerase chain reaction (PCR) and ligase chain reaction (LCR) are used as diagnostic techniques.
7. **Immunodiagnosis:** Serological tests are not useful in diagnosis.

Q. 5. Write a short note on serologic markers for HBV infection. (TNMGR, Sept. 2002)

Ans. Specific diagnosis of hepatitis B rests on the serological demonstration of the viral markers.

1. **HBsAg:** The first marker to appear in blood after infection, being detectable even before elevation of transaminases and onset of clinical illness. It remains in circulation throughout the symptomatic course of the disease. It disappears within about 2 months of the start of disease, but may sometime lasts for 6 months and beyond. When it is no longer detectable, its antibody, anti-HBs appears and remains for very long periods.
2. **HBcAg:** It is not demonstrable in circulation because it is enclosed within the HBsAg coat but its antibody; anti-HBc appears in serum a week or two after the appearance of HBsAg. It is the earliest antibody marker to be seen in blood. As anti-HBc remains life long, it serves as a useful indicator of prior infection with HBV, even after all the other viral markers become undetectable.
3. **HBeAg:** It appears in blood concurrently with HBsAg, or soon afterwards. Circulating HBeAg is an indicator of active intrahepatic viral replication and the presence in blood of DNA polymerase, HBV DNA and virions, reflecting high infectivity. The disappearance of HBeAg is followed by the appearance of anti-He.

For the diagnosis of HBV infection, detection of HBsAg in blood is necessary. The simultaneous presence of IgM anti-HBc indicates recent infection and the presence of IgG remote infection. HBeAg provides information about relative infectivity. The presence of anti-HBs without any other serological virus marker indicates immunity following vaccination. Like HBeAg, HBV DNA is also an indicator of viral replication and infectivity. Molecular methods such as DNA hybridization and PCR, at present used for HBV DNA testing are highly sensitive and quantitative.

Q. 6. Write a short note on coagulase test.

(TNMGR, April 2003)

Ans. Coagulase is an extracellular enzyme secreted into the medium. Coagulase test is the standard criteria for

the identification of *Staph. aureus* isolates. Coagulase test is done by two methods:

1. **Tube coagulase tests:** This test detects free coagulase. About 0.1 ml of a young broth culture or agar culture suspension of the isolate is added to about 0.5 ml of human or rabbit plasma in a narrow test tube. EDTA, oxalate or heparin may be used as the anticoagulant for preparing the plasma. Positive and negative controls are also set up. The tubes are incubated in a water bath at 37°C for 3–6 hours. If positive, the plasma clots and does not flow when the tube is tilted.
2. **Slide test:** This detects bound coagulase and is much simpler and usually gives results parallel with the tube test. When there is divergence, the tube test will be the deciding factor. In this test, the isolate is emulsified in a drop of saline on a slide. After checking for absence of auto-agglutination, a drop of human or rabbit plasma is added to the emulsion and mixed. Prompt clumping of the cocci indicates a positive test. Positive and negative controls also are set up.

Q. 7. Classify spirochetes. Describe the clinical features and laboratory diagnosis of syphilis.

(TNMGR, March 2007)

Q. Write a short note on lab diagnosis of syphilis.

(TNMGR, March 2009)

Ans. Classification

- a. *Spirochetaceae:* Spirochaeta, Cristispira, Treponema, Borrelia.
- b. *Leptospiraceae:* Leptospira.

Clinical Features of Syphilis

1. **Primary syphilis:** Chancre formation at the site of entry.
2. **Secondary syphilis:** Roseolar or papular skin rashes, mucous patches in the oropharynx, condylomata at the mucocutaneous junctions.
3. Latent syphilis.
4. **Tertiary syphilis:** Cardiovascular lesions, chronic granulomata, and meningovascular lesions.
5. **Congenital syphilis:** Hutchinson's triad.

Laboratory Diagnosis

A. Microscopy

1. Dark ground microscopy.
2. Direct fluorescent antibody test.

B. Serological tests

- i. **Reagin antibody tests:** Kahn test, VDRL test, rapid plasma reagin test.

- ii. *Group specific treponemal tests*: Reiter protein complement fixation test.
- iii. *Specific Treponema pallidum tests*: *Treponema pallidum* immobilization test, fluorescent treponemal antibody test, *Treponema pallidum* hemagglutination assay.

Q. 8. Write a short note on VDRL test.

(TNMGR, Aug. 2004)

Ans. VDRL (venereal disease research laboratory) test is used as serological test for the diagnosis of syphilis. In this test, the inactivated serum (serum heated at 56°C for 30 minutes) is mixed with cardiolipin antigen on a special slide and rotated for four minutes. Cardiolipin remains as uniform crystals in normal serum but forms visible clumps on combining with reagin antibody. The reaction is read under a low power microscope. By testing serial dilutions, the antibody titer can be determined. The results are reported qualitatively as 'reactive', 'weak reactive' or not reactive.' For quantitative reporting, the reciprocal of the end point is given as the titer, for example 'reactive 4 dilution' or 'titer 4.' VDRL test can be used for testing CSF also, but not plasma. CSF need not be heated prior to the test.

Modifications of VDRL test

1. *Rapid plasma reagin (RPR)*: This test is the most popular. It uses VDRL antigen containing fine carbon particles.
2. *Automated RPR test*: For large scale tests.
3. *Automated VDRL-ELISA test*: Measure IgG and IgM antibodies separately and is suitable for large scale testing of sera.

Q. 9. Write a short note on antibiotic sensitivity test.

(TNMGR, Sept. 1997; April 2015)

Ans. Antibiotic sensitivity tests are used to determine the susceptibility of isolates of pathogenic bacteria to antibiotics that are likely to be used in treatment. These are of two types:

a. Diffusion tests: The drug is allowed to diffuse through a solid medium so that a gradient is established, the concentration being highest near the site of application of the drug and decreasing with distance. The test bacterium is seeded on the medium and its sensitivity to the drug determined from the inhibition of its growth.

Methods used for the application of the drug

- i. Ditches or holes cut in the medium.
- ii. By adding to hollow cylinders (heaty cups).
- iii. Filter paper discs, impregnated with antibiotics—most commonly used method.

1. **Disc diffusion method** uses filter paper discs, 6.0 mm in diameter charged with appropriate concentrations of the drugs. A suitable dilution of a broth culture or a broth suspension of the test bacterium is flooded on the surface of a solid medium (Mueller-Hinton agar or nutrient agar). After drying the plate (37°C for 30 mins), antibiotic discs are applied with sterile forceps. After overnight incubation, the degree of sensitivity is determined by measuring the zones of inhibition of growth around the discs.

2. **Primary disc diffusion method** gives results fast as the swab is directly inoculated uniformly on the surface of a plate and discs applied.

3. **Epsilometer or E test** uses an absorbent strip with a known gradient of drug concentrations along its length. When the strip is placed on the agar plate seeded with the test bacterium, antibiotic diffuse into the medium.

b. Dilution test: In this, serial dilutions of the drug are prepared and inoculated with the test bacterium. Dilution tests are generally employed when the therapeutic dose is to be regulated accurately, for tests on slow growing bacteria, and when small degrees of resistance are to be demonstrated.

1. *Tube dilution method:* Serial dilutions of the drug in broth are taken in tubes and a standardized suspension of test bacterium inoculated. After overnight incubation, the minimum inhibitory concentration (MIC) is read by noting the lowest concentration of the drug that inhibits growth.

2. *Agar dilution method:* It is more convenient when several strains are to be tested at the same time. In this, serial dilutions of the drug are prepared in agar and poured into plates.

Q. 10. Write a short note on ELISA.

(TNMGR, March, 2002)

Ans.

In ELISA, the enzyme is linked to an antibody and used to detect and measure other antibodies and antigens. An enzyme conjugated with antibody reacts with a colorless substrate to generate a colored reaction product. Such a substrate is called chromogenic substrate.

Principle of ELISA

1. Solid phase amino assay is widely used, which refers to binding of either antigen or antibody to a variety of solid materials such as polyvinyl or polycarbonate wells or membranes of polyacrylamide, paper or plastic or metal beads or some other solid matrix.

2. Antigens and antibodies can be covalently attached to an active enzyme with the resulting complexes still fully functional. Enzyme activity is used to measure the quantity of antigen or antibody present in the test sample.

In ELISA, the enzyme act on the substrate to produce color in a positive test. It can be used for detection of antigen or antibody. The test can be done in polystyrene tubes (macro-ELISA) or polyvinyl microtiter plates (micro-ELISA).

1. Sandwich ELISA

It is most frequently used for detecting microbial antigen. It is of two types:

- a. *Single antibody or direct sandwich ELISA*: In this technique, the antibody is immobilized on a microtiter well. The test sample is then exposed to the solid phase antibody to which the antigen, if present will bind. After the well is washed, a second enzyme-linked antibody specific for test antigen is added. The conjugated antibody will react with the antigen held to the solid phase by the first antibody, forming an antibody-antigen-antibody sandwich on the solid phase. After any free second antibody is removed by washing, substrate is added and the colored reaction product is measured.
- b. *Double antibody or indirect sandwich ELISA*: It is used for the detection of antigens. In this, specific antibody is placed in wells of microtiter plate. The antibody is absorbed onto the walls, coating and sensitizing the plate. A test antigen is then added to each well. If the antigen reacts with the antibody, the antigen is retained when the well is washed to remove unbound antigen. An antibody enzyme conjugate specific for the antigen is then added to each well. The final complex is formed of an outer antibody—enzyme, middle antigen, and inner antibody.

2. Indirect ELISA

It detects antibodies. For antibody detection, the wells of microtiter plate are coated with antigen. Sera to be tested are added in these coated wells. If antibody is present in specimen, it binds to coated antigen. To detect this, antigen-antibody reaction, a goat antihuman immunoglobulin antibody conjugated with an enzyme is added. Enzyme conjugated antihuman immunoglobulin binds to antibody. To detect this binding, a substrate is added and enzyme acts on substrate to produce color in a positive reaction. Reading of the test is done by ELISA reader. Substrates are specific for each enzyme. The enzyme (horseradish peroxidase, alkaline phosphatase) gives rise to a color change by adding specific substrate (O-phenyl-diamine

dihydrochloride for peroxidase, p-nitrophenyl phosphate for alkaline phosphatase). Alkaline phosphatase with this substrate produces a yellow color.

3. Competitive ELISA

In this, positive result shows no color whereas appearance of color indicates a negative test. There are two specific antibodies, one conjugated with enzyme and other present in serum. Competition occurs between two antibodies for same antigen. A microtiter plate wells are coated with HIV antigen. Sera to be tested are added to these wells. If antibodies are present, antigen-antibody reaction occurs. To detect this reaction, enzyme labeled specific HIV antibodies are added. These antibodies remain free and washed off during washing. Substrate is added but there is no enzyme to act on it. If serum to be tested is negative for the antibodies, antigen is there to combine with enzyme conjugated antibodies and enzyme acts on substrates to produce color.

Uses of ELISA

It has been used for the detection of antigen and antibodies of various microorganisms. Examples are:

1. Detection of HIV antibodies in serum
2. Detection of mycobacterial antibodies in tuberculosis
3. Detection of rotavirus in faces
4. Detection of hepatitis B markers in serum
5. Detection of enterotoxin of *E. coli* in faces
6. Detection of antibodies for herpes simplex (V_1 and V_2).

Variations of ELISA

1. Capture ELISA
2. Immunometric tests
3. Card method
4. Dipstick method
5. Cylinder or cassette ELISA

Q. 11. Write a short note on laboratory diagnosis of streptococcal infection. (TNMGR, Sept. 2002)

Ans. In acute infections, diagnosis is established by culture while in the non-suppurative complications, diagnosis is mainly based on the demonstration of *antibodies*. Presumptive information may be obtained by an examination of **Gram stained films** from pus and CSF. The presence of gram-positive cocci in chains is indicative of streptococcal infection.

For **cultures**, swabs should be collected undervision from the affected site and either plated immediately or sent to the laboratory in Pike's medium. The specimen is plated on blood agar and incubated 37°C anaerobically or under 5–10% CO₂. Hemolytic streptococci are

grouped by the Lancefield technique. The fluorescent antibody technique has been employed for the rapid identification of group A streptococci. Typing is required only for epidemiological purposes.

In rheumatic fever and glomerulonephritis, a retrospective diagnosis of streptococcal infection may be established by demonstrating high levels of antibody to streptococcal toxins. The usual test done is antistreptolysin O titration. ASO clues higher than 200 are indicative of prior streptococcal infection. Antideoxyribonuclease B estimation is also commonly employed. Titers higher than 300 are taken as significant. Anti-DNAase B and antihyaluronidase tests are very useful for the retrospective diagnosis of streptococcal pyoderma, for which ASO is of much less value.

The streptozyme test, a passive slide hemagglutination test using erythrocytes sensitized with a crude preparation of extracellular antigens of streptococci, is a convenient, sensitive and specific screening test. It becomes positive after nearly all types of streptococcal infections.

Q. 12. Write a short note on Koch's postulates.

(TNMGR, March 2010)

Ans. According to these, a microorganism can be accepted as the causative agent of an infectious disease only if:

1. The bacterium should be constantly associated with the lesions of the disease.
2. It should be possible to isolate the bacterium in pure culture.
3. Inoculation of such pure culture into suitable laboratory animals should reproduce the lesions.
4. It should be possible to reisolate the bacterium in pure culture from the lesions produced in the experimental animals.
5. Specific antibodies to the bacterium should be demonstrable in the serum of patients suffering from the disease.

Q. 13. Write a short note on caries activity test.

Ans. Caries activity test is defined as the test used to predict the probability of developing new or increased carious lesions over a period of time.

Ideal Requirement of Caries Activity Test

1. Should have sound theoretical basis.
2. Should have maximum correlation with clinical status.

3. Be accurate with respect to duplication of results.
4. Be simple and inexpensive.

Uses

1. To determine the need for caries control measures.
2. To act as indicator of patients cooperation.
3. To act as an aid in timing of recall appointments
4. To aid in the determination of prognosis.

Classification

a. Tests for evaluating microbiological activity

1. Lactobacillus colony count
2. Dip slide method
3. Mutans streptococci colony counts
4. Snyder's test
5. Alban's test

b. Tests for evaluating saliva defense

1. Saliva flow rate
2. Viscosity of saliva
3. Buffering capacity of saliva

Q. 14. Write a short note on DNA probes.

(TNMGR, Oct. 2013)

Ans. These are rapid, sensitive and specific diagnostic tools which could be designed because of the following characteristics of DNA:

- i. Double-stranded structure
- ii. Specific base pairing

The diagnostic reagents comprise single strand of DNA either from a known organism or synthesized in the laboratory which is conjugated with an easily detectable marker like radioactive isotope or an enzyme. This can be used to identify similar DNA in the test sample since it can combine with single strand of only complementary DNA (hybridization). If the test DNA is present in the sample, it will hybridize with the DNA probe and will become detectable because of the attached marker. Hybridization reaction can be carried out either in the solution or fixed to a solid support such as nitrocellulose or nylon fibers. The latter technique is often called **dot blot, spot blot or slot blot**.

Applications: In detection of those organisms which are difficult to culture in the laboratory. Detection of organism for which diagnostic antigens are not available. These probes provide reliable result in a short time on a large number of specimens.

1. INFLAMMATION

Q. 1. Define inflammation: List the types, stages and mediators.

(BFUHS, May 2009; MUHS, May 2009;
TNMGR, October 2012)

Q. Describe the process of acute inflammation.

(TNMGR, March 2009; Suman Vidyapeeth,
April 2010; RGUHS, Oct. 2010)

Q. Write a short note on chemical mediators of inflammation.

(TNMGR, Sept. 2010; RGUHS, May 2011)

Q. Define chronic inflammation and discuss the events of inflammation.

(TNMGR, March 2009,
April 2012)

Q. Write a short note on complement cascade.

(TNMGR, March 2009)

Q. Write a short note on cytokines.

(TNMGR, March 2007, Sept. 2008, HP,
Aug. 2010; RGUHS, Nov. 2011)

Ans. Inflammation is defined as the local response of living mammalian tissues to injury due to any agent. It is a body defense reaction in order to eliminate or limit the spread of injurious agent, followed by removal of the necrosed cells and tissues.

Signs of inflammation: The Roman writer Celsus in 1st century AD named the famous 4 cardinal signs of inflammation as: Rubor (redness); tumor (swelling); calor (heat); and dolor (pain). Fifth sign—functio laesa (loss of function) was later added by Virchow.

Types of Inflammation

A. Acute Inflammation

It is of short duration (lasting less than 2 weeks). The main features of acute inflammation are:

1. Accumulation of fluid and plasma at the affected site
2. Intravascular activation of platelets
3. Polymorphonuclear neutrophils as inflammatory cells.

B. Chronic Inflammation

It is of longer duration and occurs either after the causative agent of acute inflammation persists for a long time, or the stimulus is such that it induces chronic inflammation from the beginning. The characteristic feature of chronic inflammation is presence of chronic inflammatory cells such as lymphocytes, plasma cells and macrophages, granulation tissue formation, and in specific situations as granulomatous inflammation.

A. Acute inflammation: It can be divided into the following two events:

- i. Vascular events
- ii. Cellular events

i. Vascular Events

a. Hemodynamic changes

1. Immediate vascular response is of **transient vasoconstriction** of arterioles (initial 3–5 minutes).
2. Next follows persistent **progressive vasodilatation**, which results in increased blood volume in the area, responsible for redness and warmth at the site (within half an hour of injury).
3. Progressive vasodilatation may elevate the local hydrostatic pressure resulting in transudation of fluid into the extracellular space (swelling at the site).
4. **Slowing or stasis of microcirculation** follows which causes increased concentration of red cells.
5. It is followed by leucocytic margination or peripheral orientation of leukocytes (mainly neutrophils), and then move and migrate through the gaps between the endothelial cells into the extravascular space. This process is known as **emigration**.

- b. **Altered vascular permeability:** Initially, there is escape of fluid in the spaces due to vasodilatation and consequent elevation in hydrostatic pressure. This is transudate in nature. In inflamed tissues, the endothelial lining of microvasculature becomes leakier, resulting in excessive outward flow of fluid into the interstitial compartment which is exudative inflammatory edema.

Mechanisms of increased vascular permeability

- i. Contraction of endothelial cells.
- ii. Retraction of endothelial cells.
- iii. Direct injury to endothelial cells.
- iv. Endothelial injury mediated by leukocytes.
- v. Leakiness in neovascularization.

ii. Cellular Events

The cellular phase of inflammation consists of 2 processes:

- a. **Exudation of leukocytes:** The changes leading to migration of leukocytes are as follows:

1. **Changes in the formed elements of blood:** Initial increase in the blood flow is followed by stasis of bloodstream, which leads to changes in the normal axial flow of blood. The central stream of cells widens and peripheral plasma zone becomes narrower because of loss of plasma by exudation. This phenomenon is known as **margination**. As a result, the neutrophils of the central column come close to the vessel wall; this is known as **pavementing**.
2. **Rolling and adhesion:** Peripherally margined and paved neutrophils slowly roll over the endothelial cells lining the vessel wall (rolling phase). This is followed by the transient bond between the leukocytes and endothelial cells becoming firmer (adhesion phase).
3. **Emigration:** After sticking of neutrophils to endothelium, the neutrophils gets lodged between the endothelial cells and basement membrane, cross the basement membrane, escape out into the extravascular space; this is known as **emigration**. Simultaneous to emigration, escape of red cells through gaps between the endothelial cells, **diapedesis**, takes place.
4. **Chemotaxis:** The chemotactic factor-mediated transmigration of leukocytes after crossing several barriers to reach the interstitial tissues is called **chemotaxis**. The following agents act as potent chemotactic substances or chemokines for neutrophils:

- i. Leukotrienes B₄ (LT-B₄)
- ii. Components of complement system
- iii. Cytokines (interleukins)
- iv. Soluble bacterial products

- b. **Phagocytosis:** Phagocytosis is defined as the process of engulfment of solid particulate material by the cells (cell-eating). There are 2 main types of phagocytic cells: (i) Polymorphonuclear neutrophils (PMNs), sometimes called as microphages. (ii) Circulating monocytes and fixed tissue mononuclear phagocytes, commonly called as macrophages. The process of phagocytosis involves the following 3 steps:

1. **Recognition and attachment:** Phagocytosis is initiated by the expression of surface receptors on macrophages which recognize microorganisms. Phagocytosis is further enhanced when the microorganisms are coated with specific proteins, opsonins. Opsonins establish a bond between bacteria and the cell membrane of phagocytic cell. For example, IgG opsonin, C3b opsonin, lectins.
2. **Engulfment:** This is accomplished by formation of cytoplasmic pseudopods around the particle, enveloping it in a phagocytic vacuole or phagosome, which fuses with one or more lysosomes of the cell and form bigger vacuole called phagolysosome.
3. **Killing and degradation:** The microorganisms after being killed by anti-bacterial substances are degraded by hydrolytic enzymes. Disposal of microorganisms can proceed by following mechanisms:

a. Intracellular mechanisms

- i. Oxidative bactericidal mechanism by oxygen free radicals.
 - a. MPO-dependent.
 - b. MPO-independent.
- ii. Oxidative bactericidal mechanism by lysosomal granules.
- iii. Non-oxidative bactericidal mechanism.

b. Extracellular mechanisms

- i. Degranulation of macrophages and neutrophils leads to proteolysis outside the cells as well.
- ii. immune-mediated lysis of microbe—cytolysis, antibody-mediated lysis and by cell-mediated cytotoxicity.

Chemical mediators of inflammation (permeability factors or endogenous mediators of increased vascular permeability).

Cell-derived mediators

1. Vasoactive amines (histamine—vasodilatation, increased vascular permeability, itching and pain; 5-hydroxytryptamine—same, less potent; neuropeptides—as substance-P, neurokinin A, vasoactive intestinal polypeptide (VIP) and somatostatin—increased vascular permeability, transmission of pain stimuli).
2. Arachidonic acid metabolites (eicosanoids)
 - i. Metabolites via cyclooxygenase pathway (prostaglandins—increased venular permeability, vasodilatation and bronchodilatation and inhibit inflammatory cell function; thromboxane A_2 —platelet aggregation; prostacyclin—vasodilatation, inhibits platelet aggregation, resolvins).
 - ii. Metabolites via lipo-oxygenase pathway (5-HETE—chemotactic, leukotrienes—smooth muscle contraction; lipoxins—counterbalance actions of leukotrienes).
3. Lysosomal components (from PMNs—3 types of granules: primary or azurophil, secondary or specific, and tertiary; macrophages—granules releases acid proteases, collagenase, elastase and plasminogen activator).
4. Platelet activating factor (PAF)—platelet aggregation, chemotaxis.
5. Cytokines (IL-1, TNF- α , TNF- β , IFN- γ , chemokines).
6. Free radicals (oxygen metabolites, nitric oxide).

Plasma-derived mediators (plasma proteases): Products of:

1. *The kinin system*: Bradykinin—smooth muscle contraction; vasodilatation; increased vascular permeability; and pain.
2. *The clotting system*: Fibrinopeptides—increased vascular permeability; chemotaxis for leukocyte; and anticoagulant activity.
3. *The fibrinolytic system*: Plasmin—activation of factor XII stimulates the kinin system to generate bradykinin; splits off complement C3 to form C3a; degrades fibrin to form fibrin split products (FSP) which increase vascular permeability and are chemotactic to leukocytes.
4. The complement system.

Cytokines: Cytokines are polypeptide substances produced by activated lymphocytes (lymphokines) and activated monocytes (monokines). These agents may act on 'self' cells producing them or on other cells. Major cytokines acting as mediators of inflammation are: interleukin-1 (IL-1), tumor necrosis factor (TNF)- α and β , interferon (IFN)- γ , and chemokines (IL-8, PF-4). IL-1

and TNF- α are formed by activated macrophages while TNF- β and IFN- γ are produced by activated T cells. The chemokines include interleukin 8 (released from activated macrophages) and platelet factor-4 from activated platelets, both of which are potent chemo-attractant for inflammatory cells. The actions of various cytokines as mediator of inflammation are as under:

- i. IL-1 and TNF- α , TNF- β induce endothelial effects in the form of increased leukocyte adherence, thrombogenicity, elaboration of other cytokines, fibroblastic proliferation and acute phase reactions.
- ii. IFN- γ causes activation of macrophages and neutrophils and is associated with synthesis of nitric acid synthase.
- iii. Chemokines are a family of chemoattractant for inflammatory cells and include: IL-8 chemotactic for neutrophils; platelet factor-4 chemotactic for neutrophils, monocytes and eosinophils; MCP-1 chemotactic for monocytes; and eotaxin chemotactic for eosinophils.

Complement system: The activation of complement system can occur either:

- i. By classic pathway through antigen-antibody complexes.
- ii. By alternate pathway via non-immunologic agents such as bacterial toxins, cobra venoms and IgA.

Complement system on activation by either of these two pathways yields activated products which include anaphylatoxins (C3a, C4a and C5a), and membrane attack complex (MAC), i.e. C5b–C9.

The actions of activated complement system in inflammation are

- i. C3a, C5a, C4a (anaphylatoxins) activate mast cells and basophils to release of histamine, cause increased vascular permeability causing edema in tissues, augments phagocytosis.
- ii. C3b is an opsonin.
- iii. C5a is chemotactic for leukocytes.
- iv. Membrane attack complex (C5b–C9) is a lipid dissolving agent and causes holes in the phospholipid membrane of the cell.

Factors determining variation in inflammatory response

1. Factors involving the organisms
 - i. Type of injury and infection.
 - ii. Virulence.
 - iii. Dose.
 - iv. Portal of entry.
 - v. Product of organisms.

2. Factors involving the host
 - i. Systemic diseases
 - ii. Immune status of host
 - iii. Congenital neutrophil defects
 - iv. Leucopenia
 - v. Site or type of tissue involved.
 - vi. Local host factors.
3. *Type of exudation*: The appearance of escaped plasma determines the morphologic type of inflammation as:
 - i. Serous
 - ii. Fibrinous
 - iii. Purulent
 - iv. Hemorrhagic
 - v. Catarrhal

Morphology of acute inflammation: A few morphologic varieties of acute inflammation are:

1. Pseudomembranous inflammation
2. Ulcer
3. Suppuration (abscess formation)
4. Cellulitis
5. Bacterial infection of the blood. This includes:
 - i. *Bacteremia*: Presence of small number of bacteria in the blood which do not multiply significantly.
 - ii. *Septicemia*: Presence of rapidly multiplying, highly pathogenic bacteria in the blood, generally accompanied by systemic effects like toxemia, multiple small hemorrhages, neutrophilic leukocytosis and disseminated intravascular coagulation (DIC).
 - iii. *Pyemia*: It is the dissemination of small septic thrombi in the blood which cause their effects at the site where they are lodged. This can result in pyemic abscesses or septic infarcts.

Systemic effects of acute inflammation: These include: Fever, leukocytosis and lymphangitis lymphadenitis, shock, DIC bleeding and death.

Fate of acute inflammation

1. Resolution
2. Healing
3. Suppuration
4. Chronic inflammation.

Chronic inflammation: It is defined as prolonged process in which tissue destruction and inflammation occur at the same time.

Chronic inflammation can be caused by one of the following 3 ways

1. Chronic inflammation following acute inflammation.
2. Recurrent attacks of acute inflammation.
3. Chronic inflammation starting *de novo*.

General features of chronic inflammation: Following general features characterize any chronic inflammation:

1. **Mononuclear cell infiltration:** Chronic inflammatory lesions are infiltrated by mononuclear inflammatory cells like phagocytes (circulating monocytes, tissue macrophages, epithelioid cells and sometimes, multinucleated giant cells) and lymphoid cells. Other chronic inflammatory cells include lymphocytes, plasma cells, eosinophils and mast cells.
2. **Tissue destruction or necrosis:** This is brought about by activated macrophages which release a variety of biologically active substances, e.g. protease, elastase, collagenase, lipase, etc.
3. **Proliferative changes:** Healing by fibrosis and collagen lying takes place.

Systemic effects of chronic inflammation

1. Fever
2. Anemia
3. Leukocytosis
4. Elevated ESR
5. Amyloidosis

Types of chronic inflammation

1. *Non-specific*: When the irritant substance produces a nonspecific chronic inflammatory reaction with formation of granulation tissue and healing by fibrosis, e.g. chronic osteomyelitis, chronic ulcer.
2. *Specific*: When the injurious agent causes a characteristic histologic tissue response, e.g. tuberculosis, leprosy, syphilis.

However, histological features are used for classifying chronic inflammation into 2 corresponding types:

1. *Chronic non-specific inflammation*: It is characterized by non-specific inflammatory cell infiltration, e.g. chronic osteomyelitis, lung abscess. A variant of this type is chronic suppurative inflammation in which infiltration by polymorphs and abscess formation are additional features, e.g. actinomycosis.
2. *Chronic granulomatous inflammation*: It is characterized by formation of granulomas, e.g. tuberculosis, leprosy, syphilis, actinomycosis, sarcoidosis, etc.

Q. 2. Write a short note on giant cells.

(TNMGR, Sept. 2007)

Ans.

a. Giant cells in inflammation

- i. *Foreign body giant cells*: These contain numerous nuclei (up to 100) which are uniform in size and shape and resemble the nuclei of macrophages. For example, chronic infective granulomas, leprosy and tuberculosis.

- ii. *Langhans' giant cells*: These nuclei are arranged either around the periphery in the form of horseshoe or ring, or are clustered at the two poles of the giant cell. For example, tuberculosis and sarcoidosis.
- iii. *Touton giant cells*: These multinucleated cells have vacuolated cytoplasm due to lipid content, e.g. in xanthoma.
- iv. *Aschoff giant cells*: These multinucleate giant cells are derived from cardiac histiocytes and are seen in rheumatic nodule.

b. Giant cells in tumors

- i. *Anaplastic cancer giant cells*: These are larger, have numerous nuclei which are hyperchromatic and vary in size and shape. For example, carcinoma of the liver, various soft tissue sarcomas, etc.
- ii. *Reed-Sternberg cells*: These are also malignant tumor giant cells which are generally binucleate, seen in Hodgkin's lymphomas.
- iii. *Giant cell tumor of bone*: This tumor of the bones has uniform distribution of osteoclastic giant cells spread in the stroma.

Q. 3. Write a short note on granulomatous Inflammation. (TNMGR, Nov. 2001)

Q. Write a short note on histologic picture of granuloma. (TNMGR, March 2007, Sept. 2010)

Ans. Granuloma is defined as a circumscribed, tiny lesion, about 1 mm in diameter, composed predominantly of collection of modified macrophages called epithelioid cells, and rimmed at the periphery by lymphoid cells.

Pathogenesis of Granuloma

The sequence in evolution of granuloma:

1. **Engulfment by macrophages**: Macrophages and monocytes engulf the antigen but these cells fail to digest and degrade the antigen, and instead undergo morphologic changes to epithelioid cells.
2. **CD4+ T cells**: Macrophages, present the antigen to CD4+ T-lymphocytes. These lymphocytes get activated and elaborate lymphokines (IL-1, IL-2, interferon- γ , TNF- α).
3. **Cytokines**: Various cytokines formed by activated CD4+ T cells and also by activated macrophages perform the following roles:
 - i. IL-1 and IL-2 stimulate proliferation of more T cells.
 - ii. Interferon- γ activates macrophages.

iii. TNF- α promotes fibroblast proliferation and activates endothelium to secrete prostaglandins which have role in vascular response in inflammation.

iv. Growth factors (transforming growth factor- β , platelet derived growth factor) elaborated by activated macrophages stimulate fibroblast growth.

Composition of granuloma: In general, a granuloma has the following structural composition:

1. **Epithelioid cells**: These are modified macrophages/histiocytes, with slipper-shaped nucleus, and pale staining abundant cytoplasm with hazy outlines and are weakly phagocytic.
2. **Multinucleate giant cells**: Multinucleate giant cells are formed by fusion of adjacent epithelioid cells and may have 20 or more nuclei. These nuclei may be arranged at the periphery like horseshoe or ring, or are clustered at the two poles (Langhans' giant cells), or they may be present centrally (foreign body giant cells). These giant cells are weakly phagocytic but produce secretory products which help in removing the invading agents.
3. **Lymphoid cells**: As a cell-mediated immune reaction to antigen, the host response by lymphocytes is integral to composition of a granuloma.
4. **Necrosis**: Necrosis may be a feature of some granulomatous conditions, e.g. central caseation necrosis of tuberculosis.
5. **Fibrosis**: Fibrosis is a feature of healing by proliferating fibroblasts at the periphery of granuloma.

The classical example of granulomatous inflammation is the tissue response to tubercle bacilli which is called tubercle seen in tuberculosis.

Q. 4. Write a short note on primary complex. (TNMGR, April 2000; BFUHS, May 2011)

Ans. Primary complex or Ghon's complex is the lesion produced in the tissue of portal of entry with foci in the draining lymphatic vessels and lymph nodes. The most commonly involved tissues for primary complex are lungs and hilar lymph nodes. Other tissues which may show primary complex are tonsils and cervical lymph nodes, and in small intestine and mesenteric lymph nodes. Primary complex or Ghon's complex in lungs consists of 3 components:

1. **Pulmonary component**: Lesion in the lung is the primary focus or Ghon's focus. It is 1–2 cm solitary area of tuberculous pneumonia located peripherally under a patch of pleurisy, in any part of the lung. Microscopically, the lung lesion consists of tuberculous granulomas with caseation necrosis.

2. **Lymphatic vessel component:** The lymphatics draining the lung lesion contain phagocytes containing bacilli and may develop beaded, miliary tubercles along the path of hilar lymph nodes.
3. **Lymph node component:** The lymph nodes are enlarged (hilar and tracheobronchial lymph nodes), matted. Microscopically, the lesions are characterized by extensive caseation, tuberculous granulomas and fibrosis. Nodal lesions are potential source of re-infection later.

In the case of primary tuberculosis of the alimentary tract due to ingestion of tubercle bacilli, a small primary focus is seen in the intestine with enlarged mesenteric lymph nodes producing tabes mesenterica. The enlarged and caseous mesenteric lymph nodes may rupture into peritoneal cavity and cause tuberculous peritonitis.

Q. 5. Write a short note on hemochromatosis.

(TNMGR, April 2001, March 2010)

Ans. Hemochromatosis is an iron-storage disorder in which there is excessive accumulation of iron in parenchymal cells with eventual tissue damage and functional insufficiency of organs.

The condition is characterized by a triad of features—micronodular pigment cirrhosis, diabetes mellitus and skin pigmentation. On the basis of the last two features, the disease has also come to be termed as '**bronze diabetes**'. Males predominate and manifest earlier than females. Exists in 2 main forms:

1. **Idiopathic (primary, genetic):** An autosomal recessive disorder, associated with overexpression of HFE gene located on chromosome 6 close to the HLA gene locus.
2. **Secondary (acquired):** Secondary to other diseases such as thalassemia, sideroblastic anemias, alcoholic cirrhosis or multiple transfusions.

Etiopathogenesis

In **idiopathic or hereditary hemochromatosis**, the defect lie at the intestinal mucosal level causing excessive iron absorption, or at the post-absorption excretion level leading to excessive accumulation of iron.

In **secondary or acquired hemochromatosis**, excessive accumulation of iron due to acquired causes like ineffective erythropoiesis, defective hemoglobin synthesis, multiple blood transfusions and enhanced absorption of iron due to alcohol consumption.

Clinical Features

1. Characteristic bronze pigmentation of the skin
2. Diabetes mellitus

3. Hepatic—cirrhosis, carcinoma
4. Cardiac dysfunction
5. Arthropathy
6. Hypogonadism

Q. 6. Write a short note on free radicals.

(TNMGR, April 2012)

Ans. Although oxygen is the lifeline of all cells and tissues, its molecular forms as reactive oxygen radicals or reactive oxygen species can be most devastating for the cells.

Mechanism of oxygen free radical generation: Normally, metabolism of the cell involves generation of ATP by oxidative process in which biradical oxygen (O_2) combines with hydrogen atom (H) and in the process forms water (H_2O). Oxygen free radicals are the intermediate chemical species having unpaired oxygen in their outer orbit.

1. Superoxide oxygen (O_2^-): One electron
2. Hydrogen peroxide (H_2O_2): Two electrons
3. Hydroxyl radical (OH^\cdot): Three electrons
4. Release of superoxide free radical
5. Nitric oxide (NO)
6. Hypochlorous acid (HOCl).
7. Exogenous sources—tobacco and industrial pollutants.

Cytotoxicity of oxygen free radicals: Free radicals are highly destructive to the cell since they have electron-free residue and thus bind to all molecules of the cell; this is termed **oxidative stress**. Free radicals may produce membrane damage by the following mechanisms:

- i. Lipid peroxidation
- ii. Oxidation of proteins
- iii. DNA damage
- iv. Cytoskeletal damage

Conditions with free radical injury: They play a role in many forms of cell injury:

- i. Ischemic reperfusion injury
- ii. Ionizing radiation by causing radiolysis of water
- iii. Chemical toxicity
- iv. Chemical carcinogenesis
- v. Hyperoxia (toxicity due to oxygen therapy)
- vi. Cellular aging
- vii. Killing of microbial agents
- viii. Inflammatory damage
- ix. Destruction of tumor cells
- x. Atherosclerosis.

Q. 7. Discuss the nature and pathogenesis of various types of amyloidosis. (TNMGR, March 2010)

Ans. Amyloidosis is the term used for a group of diseases characterized by extracellular deposition of fibrillar proteinaceous substance called amyloid having common morphological appearance, staining properties and physical structure but with variable protein (or biochemical) composition.

Physical and chemical nature of amyloid: Amyloid is composed of 2 main types of complex proteins:

i. **Fibril proteins (95%):** The fibrils have cross- β -pleated sheet configuration which gives the characteristic staining properties of amyloid with Congo red and birefringence under polarizing microscopy. Based on these features amyloid is also referred to as β -fibrillosis. These proteins can be categorized as under:

1. AL (amyloid light chain) protein
2. AA (amyloid associated) protein
3. Other proteins—transthyretin (TTR). $A\beta$ 2-microglobulin ($A\beta$ 2M). β -amyloid protein ($A\beta$). Immunoglobulin heavy chain amyloid (AH), Amyloid from hormone precursor proteins. Amyloid of prion protein (APrP).

ii. **Non-fibrillar components (5%)**

1. Amyloid P (AP)—component.
2. Apolipoprotein-E (apoE).
3. Sulfated glycosaminoglycans (GAGs).
4. α -1 anti-chymotrypsin.
5. Protein X.
6. Other components—components of complement, proteases, and membrane constituents.

Pathogenesis

1. Pool of amyloidogenic precursor protein is present in circulation in different clinical settings and in response to stimuli.
2. A nidus for fibrillogenesis, to stimulate deposition of amyloid protein is formed. This alteration involves changes and interaction between basement membrane proteins and amyloidogenic protein.
3. Partial degradation or proteolysis occurs prior to deposition of fibrillar protein which may occur in macrophages or reticuloendothelial cells.
4. The non-fibrillar components facilitate in aggregation of proteins and protein folding leading to fibril formation, substrate adhesion and protection from degradation.

Classification

- i. **Based on cause:** Primary and secondary.
- ii. **Based on extent of amyloid deposition**

1. Systemic (generalized)
2. Localized

a. Systemic (generalized) amyloidosis

1. **Primary (AL):** Plasma cell dyscrasias.
2. **Secondary/reactive/ inflammatory (AA):** Chronic infections, autoimmune disorders, tumors.
3. **Hemodialysis-associated ($A\beta$ 2M):** Chronic renal failure.
4. **Heredofamilial (ATTR, AA, others):** Hereditary polyneuropathic, Mediterranean fever.

b. Localized amyloidosis

1. Senile cardiac (ATTR).
2. Senile cerebral ($A\beta$, APrP).
3. Endocrine (hormone precursors)—medullary carcinoma of the thyroid.
4. Tumor-forming (AL).

Staining Characteristics

1. **Stain on gross:** Lugol's iodine imparts mahogany brown color to the amyloid containing area which on addition of dilute sulfuric acid turns blue.
2. **H and E:** Extracellular, homogeneous, structureless and eosinophilic hyaline material.
3. **Metachromatic stains (rosaniline dyes):** Methyl violet and crystal violet which impart rose-pink coloration.
4. **Congo red and polarized light:** Pink red color. In polarized light, the amyloid characteristically shows apple-green birefringence.
5. **Fluorescent stains:** Thioflavin-T binds to amyloid and fluoresce yellow under ultraviolet light.
6. **Immunohistochemistry:** Amyloid can be classified by immunohistochemical stains. Most useful in confirmation for presence of amyloid of any type is anti-AP stain.
7. **Non-specific stains**
 - i. **Standard toluidine blue:** This method gives orthochromatic blue color to amyloid.
 - ii. **Alcian blue:** It imparts blue-green color.
 - iii. **Periodic acid-Schiff (PAS):** It is used for demonstration of carbohydrate content.

Diagnosis

1. Biopsy.
2. *In vivo* Congo red test.
3. **Other tests:** Protein electrophoresis, immunoelectrophoresis of urine and serum, and bone marrow aspiration.

Morphologic features of amyloidosis of organs: Most commonly amyloid deposits appear at the contacts

between the vascular spaces and parenchymal cells, in the extracellular matrix and within the basement membranes of blood vessels. Grossly, the affected organ is usually enlarged, pale and rubbery. Cut surface shows firm, waxy and translucent parenchyma which takes positive staining with the iodine test. Microscopically, the deposits of amyloid are found in the extracellular locations, initially in the walls of small blood vessels producing microscopic changes and effects, while later the deposits are in large amounts causing macroscopic changes and effects of pressure atrophy. Amyloidosis of kidneys is most common and most serious. Amyloidosis of spleen shows two patterns: (1) Sago spleen; (2) Lardaceous spleen.

Q. 8. What do you understand by the term fibromatosis? Give a brief account of the entities you would include under these headings.

(TNMGR, March 2010)

Ans. Fibromatosis is the term used for tumor-like lesions of fibrous tissue which continue to proliferate actively and may be difficult to differentiate from sarcomas. It is broadly grouped as under:

- a. **Infantile or juvenile fibromatoses:** Fibrous hamartoma of infancy, fibromatosis colli, diffuse infantile fibromatosis, juvenile aponeurotic fibroma, juvenile nasopharyngeal angiofibroma and congenital (generalized and solitary) fibromatosis.
- b. **Adult type of fibromatoses:** Palmar and plantar fibromatosis, nodular fasciitis, cicatricial fibromatosis, keloid, irradiation fibromatosis, penile fibromatosis (Peyronie's disease), abdominal and extra-abdominal desmoids fibromatosis, and retroperitoneal fibromatosis.

Keloid: A keloid is a progressive fibrous overgrowth in response to cutaneous injury such as burns, incisions, insect bites, vaccinations and others. Keloids are found more often in blacks. Their excision is frequently followed by recurrences.

Grossly, the keloid is a firm, smooth, pink, raised patch from which extend claw-like processes (keloid-claw).

Histologically, it is composed of thick, homogeneous, eosinophilic hyalinized bands of collagen admixed with thin collagenous fibers and large active fibroblasts.

Nodular fasciitis: It is also called pseudosarcomatous fibromatosis, is a form of benign and reactive fibroblastic growth extending from superficial fascia into the subcutaneous fat, and sometimes into the subjacent muscle. The most common locations are the upper extremity, trunk and neck region of young adults. Local excision is generally curative. Grossly, the

lesion appears as a solitary well-circumscribed nodule in the superficial fascia. Microscopically, most common is a whorled or S-shaped pattern of fibroblasts present in edematous background.

Palmar and plantar fibromatoses: These fibromatoses, also called **Dupuytren-like contractures** are the most common form of fibromatoses occurring superficially. Palmar fibromatosis is more common in the elderly males occurring in the palmar fascia and leading to flexion contractures of the fingers (Dupuytren's contracture). It appears as a painless, nodular or irregular, infiltrating, benign fibrous subcutaneous lesion.

Plantar fibromatosis is a similar lesion occurring on the medial aspect of plantar arch. However, plantar lesions are less common than palmar type and do not cause contractures as frequently as palmar lesions. They are seen more often in adults and are infrequently multiple and bilateral. Essentially similar lesions occur in the shaft of the penis (**penile fibromatosis or Peyronie's disease**) and in the soft tissues of the knuckles (**knuckle pads**).

Desmoid fibromatoses: Desmoid fibromatoses or musculo-aponeurotic fibromatoses, commonly referred to as **desmoid tumors**, are of 2 types: Abdominal and extra-abdominal. Clinically, both types behave in an aggressive manner. Recurrences are frequent and multiple.

2. REPAIR AND DEGENERATION

Q. 1. Write a short note on healing by primary and secondary intention. (TNMGR, March 2007, 2008)

Q. Discuss healing of wounds and factors that delay healing of wounds. (TNMGR, March, 2007, Sept. 2008)

Q. Write in detail about the mechanism of wound healing. (Nagpur Uni., Oct. 2001; TNMGR, April 2012)

Q. Define repair. Describe the process of healing of a surgical wound. (TNMGR, April 2001, Sept. 2010)

Ans. Healing is the body response to injury in an attempt to restore normal structure and function. Healing involves 2 distinct processes:

Regeneration when healing takes place by proliferation of parenchymal cells and usually results in complete restoration of the original tissues.

Repair when healing takes place by proliferation of connective tissue elements resulting in fibrosis and scarring. At times, both the processes take place simultaneously.

a. Healing by first intention (primary union): Healing of a wound which has the following characteristics: (i) clean and uninfected; (ii) surgically incised; (iii) without much loss of cells and tissue; and (iv) edges of wound are approximated by surgical sutures. The sequence of events is as follows:

1. **Initial hemorrhage:** Immediately after injury, the space between the approximated surfaces of incised wound is filled with blood which then clots and seals the wound against dehydration and infection.
2. **Acute inflammatory response:** This occurs within 24 hours with appearance of polymorphs from the margins of incision. By 3rd day, polymorphs are replaced by macrophages.
3. **Epithelial changes:** The basal cells of epidermis from both the cut margins start proliferating and migrating towards incisional space in the form of epithelial spurs. A well-approximated wound is covered by a layer of epithelium in 48 hours. By 5th day, a multilayered new epidermis is formed which is differentiated into superficial and deeper layers.
4. **Organization:** By 3rd day, fibroblasts also invade the wound area. By 5th day, new collagen fibrils start forming which dominate till healing is completed. In 4 weeks, the scar tissue with scanty cellular and vascular elements, a few inflammatory cells and epithelialized surface is formed.
5. **Suture tracks:** Each suture track is a separate wound and incites the same phenomena as in healing of the primary wound. When sutures are removed around 7th day, much of epithelialized suture track is avulsed and the remaining epithelial tissue in the track is absorbed. However, sometimes the suture track gets infected (**stitch abscess**), or the epithelial cells may persist in the track (**implantation or epidermal cysts**). Thus, the scar formed in a sutured wound is neat due to close apposition of the margins of wound.

b. Healing by second intention (secondary union): This is defined as healing of a wound having the following characteristics: (i) open with a large tissue defect; (ii) having extensive loss of cells and tissues; and (iii) the wound is not approximated by surgical sutures but is left open.

The basic events in secondary union are similar to primary union but differ in having a larger tissue defect which has to be bridged. Hence, healing takes place from the base upwards as well as from the margins inwards. The healing by second intention is slow and results in a large, at times ugly, scar as compared to rapid healing and neat scar of primary union. The sequence of events is as follows:

1. **Initial hemorrhage:** As a result of injury, the wound space is filled with blood and fibrin clot which dries.
2. **Inflammatory phase:** There is an initial acute inflammatory response followed by appearance of macrophages which clear off the debris as in primary union.
3. **Epithelial changes:** The proliferating epithelial cells from both the margins of wound proliferate and migrate into the wound in the form of epithelial spurs along with granulation tissue from base, which fills the wound space. Pre-existing viable connective tissue is separated from necrotic material and clot on the surface, forming scab which is cast off. In time, the regenerated epidermis becomes stratified and keratinized.
4. **Granulation tissue** (main bulk of secondary healing): Granulation tissue is formed by proliferation of fibroblasts and neovascularization from the adjoining viable elements. The newly-formed granulation tissue is deep red, granular and very fragile. With time, the scar on maturation becomes pale and white due to increase in collagen and decrease in vascularity.
5. **Wound contraction:** Contraction of wound is an important feature of secondary healing, not seen in primary healing. Due to the action of myofibroblasts present in granulation tissue, the wound contracts to one-third to one-fourth of its original size.
6. **Presence of infection:** Bacterial contamination of an open wound delays the process of healing due to release of bacterial toxins that provoke necrosis, suppuration and thrombosis. Surgical removal of dead and necrosed tissue, debridement, helps in preventing the bacterial infection of open wounds.

Complications of Wound Healing

1. Infection of wound.
2. Implantation (epidermal) cyst formation.
3. Pigmentation.
4. Deficient scar formation.
5. Incisional hernia or wound dehiscence.
6. Hypertrophied scars and keloid formation.
7. Excessive contraction.
8. Neoplasia.

Q. 2. Discuss the factors affecting wound healing.

(TNMGR, Sept. 2009)

Ans.

a. Local factors

1. Infection is the most important factor acting locally which delays the process of healing.
2. Poor blood supply to wound slows healing.

3. Foreign bodies including sutures interfere with healing and cause intense inflammatory reaction and infection.
4. Movement delays wound healing.
5. Exposure to ionizing radiation delays granulation tissue formation.
6. Exposure to ultraviolet light facilitates healing.
7. Type, size and location of injury determines whether healing takes place by resolution or organization.

b. Systemic factors

1. **Age:** Wound healing is rapid in young.
2. **Nutrition:** Deficiency of constituents like protein, vitamin C (scurvy) and zinc delays the wound healing.
3. Systemic infection delays wound healing.
4. Administration of glucocorticoids has anti-inflammatory effect.
5. Uncontrolled diabetics-delay in healing.
6. Hematologic abnormalities like defect of neutrophil functions and neutropenia and bleeding disorders slow the process of wound healing.

Q. 3. Write a short note on fracture healing.

(TNMGR, March 2002, 2008; BFUHS, May 2009)

Ans. Basic events in healing of any type of fracture are:

- a. Primary union of fractures:** Occurs in few situations, when the ends of fracture are approximated by application of compression clamps. In these cases, bony union takes place with formation of medullary callus without periosteal callus formation. The patient can be made ambulatory early but there is more extensive bone necrosis and slow healing.
- b. Secondary union:** It is more common process of fracture healing. Secondary bone union is described under the following 3 headings.

i. Procallus formation

1. **Hematoma:** Bleeding from torn blood vessels fills the area surrounding the fracture and forms a loose meshwork and fibrin clot which acts as framework for subsequent granulation tissue formation.
2. **Local inflammatory response:** It occurs at the site of injury with exudation of fibrin, polymorphs and macrophages. The macrophages clear away the fibrin, red blood cells, inflammatory exudate and debris. Fragments of necrosed bone are scavenged by macrophages and osteoclasts.
3. **Ingrowth of granulation tissue:** It begins with neovascularization and proliferation of mesenchymal cells from periosteum and endosteum. A soft tissue callus is thus formed which joins

the ends of fractured bone without much strength.

4. **Callus composed of woven bone and cartilage:** It starts within the first few days. The cells of inner layer of the periosteum have osteogenic potential and lay down collagen as well as osteoid matrix in the granulation tissue. The osteoid undergoes calcification and is called **woven bone callus**. At times, callus is composed of woven bone as well as cartilage, temporarily immobilizing the bone ends. This stage is called **provisional callus** or **procallus** formation and is arbitrarily divided into external, intermediate and internal procallus.

- ii. **Osseous callus formation:** The woven bone is cleared away by incoming osteoclasts and the calcified cartilage disintegrates. In their place, newly-formed blood vessels and osteoblasts invade; laying down osteoid which is calcified and lamellar bone is formed by developing haversian system concentrically around the blood vessels.

- iii. **Remodeling:** During the formation of lamellar bone, osteoblastic laying and osteoclastic removal are taking place, remodeling the united bone ends. The external callus is cleared away, compact bone (cortex) is formed in place of intermediate callus and the bone marrow cavity develops in internal callus.

Complications of fracture healing

1. Fibrous union
2. Pseudoarthrosis
3. Non-union
4. Delayed union

Q. 4. Write about healing of tooth socket following dental extraction.

(RGUHS, May 2011; TNMGR, Oct. 2012)

Q. Write a short note on bone changes after extraction of tooth.

(KLE Uni. Jan. 2009)

Ans.

A.Immediate reaction following tooth extraction

1. Blood fills the socket, coagulates, RBCs gets entrapped in the fibrin meshwork and ends of torn blood vessels become sealed off.
2. Within 24–48 hours, there is vasodilation, mobilization of leukocytes around the clot.
3. The surface of the blood clot is covered by fibrin.

B. First week wound

1. Proliferation of fibroblasts from connective tissue cells.
2. These fibroblasts grow into clot.

3. The clot forms a scaffold and begins to organize.
4. The peripheral epithelium shows proliferation.
5. The crest of alveolar bone shows osteoclastic activity.

C. Second week wound

1. The blood clot becomes organized by growth of fibroblasts growing into the fibrin meshwork.
2. New delicate capillaries penetrate to the centre of clot.
3. The remnants of periodontal ligament undergo degeneration.
4. Extensive epithelial proliferation takes place.
5. Fragments of necrotic bone get resorbed.

D. Third week wound

1. The clot becomes completely organized by maturing granulation tissue.
2. Trabeculae of uncalcified bone are formed around the periphery of socket wall.
3. The crest of alveolar bone is rounded off by osteoclastic resorption.
4. The surface of the wound becomes completely epithelized.

E. Fourth week wound

1. Continuing bone deposition and remodeling resorption, filling the alveolar socket.
2. The newly formed bone is poorly calcified.
3. Maturative remodeling continues for weeks.

Q. 5. Discuss the mechanism of repair of tissues.

(TNMGR, April 1998)

Ans. Repair occurs when healing takes place by proliferation of connective tissue elements resulting in fibrosis and scarring. Two processes are involved in repair:

1. Granulation tissue formation
2. Contraction of wounds

Repair response takes place by participation of mesenchymal cells (connective tissue stem cells, fibrocytes and histiocytes), endothelial cells, macrophages, platelets, and the parenchymal cells of the injured organ.

1. Granulation tissue formation

- a. *Phase of inflammation:* Following trauma, blood clots at the site of injury. There is acute inflammatory response with exudation of plasma, neutrophils and some monocytes within 24 hours.
- b. *Phase of clearance:* Combination of proteolytic enzymes liberated from neutrophils, autolytic enzymes from dead tissues cells, and phagocytic activity of macrophages clear off the necrotic tissue, debris and red blood cells.

c. *Phase of ingrowth of granulation tissue:* This phase consists of 2 main processes: Angiogenesis or neovascularisation, and fibrogenesis. Angiogenesis takes place under the influence of following factors: a) vascular endothelial growth factor (VEGF), b) platelet-derived growth factor (PDGF), transforming growth factor- β (TGF- β), and basic fibroblast growth factor (bFGF). The new fibroblasts originate from fibrocytes as well as by mitotic division of fibroblasts.

2. **Contraction of wounds:** The wound starts contracting after 2–3 days and the process is completed by the 14th day. During this period, the wound is reduced by approximately 80% of its original size. This occurs because of dehydration, contraction of collagen, and presence of myofibroblasts.

Q. 6. Write a short note on biopsy.

(TNMGR, Sept. 2007, April 2012)

Ans. Biopsy is defined as obtaining tissue from a living organism with the rationale of examining it under the microscope in order to establish a diagnosis based on the sample.

Uses of Biopsy

1. Diagnostic
2. Appropriate treatment planning
3. Progress of treatment
4. Extension of disease

Indications

1. Any ulcer which has been present for more than 2 weeks or one which fails to respond to therapy.
2. Any growth which has been present for more than 2 weeks.
3. White or red lesion in the oral cavity, with suspicious appearance.
4. Radiographically suspicious lesions of the jaws.
5. Inflammatory lesion that does not respond to local treatment after 2 weeks.
6. Persistent keratotic changes in surface tissue in highly suspicious sites in the oral cavity.
7. Lesion that has the clinical features of malignancy.

Biopsy Procedure

1. Selection of the area to biopsy
2. Preparation of the surgical field
3. Local anesthesia
4. The incision
5. Tissue handling
6. Suturing

Types of Biopsy

1. **Exfoliative cytology:** It is the study of cells that have been shed or removed from the epithelial surface.
2. **Oral brush biopsy:** The oral brush biopsy, using a specially devised circular bristled brush, has been designed to access and sample all epithelial layers, in conjunction with the basal cell layer and the most superficial portion of the lamina propria.
3. **Fine needle aspiration (FNA) biopsy:** Aspiration or FNA biopsy is performed with a fine needle attached to a syringe. Aspiration biopsy is often referred to as fine needle aspiration (FNA). FNA biopsy is a percutaneous (through the skin) biopsy. FNA biopsy is typically accomplished with a fine gauge needle (22 gauge or 25 gauge). FNA is the fastest and easiest method of biopsy, and the results are rapidly available. One disadvantage of FNA is that the procedure only removes very small samples of tissue or cells. If the sample is benign fluid (for example, a cyst), then the procedure is ideal.
4. **Punch biopsy:** It is typically used by dermatologists to sample skin rashes, moles and other small masses, in a similar way this technique is useful in oral mucosal biopsies. Generally, it is used in an incisional fashion for diagnostic purposes; however, larger punches may be used to excise small lesions. After a local anesthetic is injected, a biopsy punch (3 to 4 mm or 0.15 inch in diameter), is used to cut out a cylindrical piece of mucosa.
5. **Incisional biopsy:** A punch biopsy is essentially an incisional biopsy, except it is round rather than elliptical. Incisional biopsy can include the part of a lesion, or part of the affected mucosa plus part of the normal mucosa (to show the interface between normal and abnormal mucosa) for purposes of diagnosis.
6. **Excisional biopsy:** The excisional biopsy is analogous to incisional biopsy, with the exception of that entire lesion or tumor is included.
7. **Bone biopsy:** Biopsy is usually required to attain a provisional diagnosis, which may need to be confirmed by examination of the full lesion if excision follows. Biopsy may be necessary to differentiate between benign bone tumors, metastatic tumors, degenerative or congenital lesions.

Q. 7. Write a short note on cellular degeneration.

(Nagpur Uni., 1996; RGUHS, Oct. 2010; TNMGR, April 2012)

Ans. Degeneration is morphology of reversible cell injury. Following are the morphologic forms of reversible cell injury.

1. Hydropic change: Hydropic change means accumulation of water within the cytoplasm of the cell. Other synonyms used are cloudy swelling (for gross appearance of the affected organ) and vacuolar degeneration (due to cytoplasmic vacuolation).

Etiology: Acute and subacute cell injury from various etiologic agents such as bacterial toxins, chemicals, poisons, burns, high fever, intravenous administration of hypertonic glucose or saline, etc.

Pathogenesis: Cloudy swelling results from impaired regulation of sodium and potassium at the level of cell membrane. This leads to rapid flow of water into the cell to maintain iso-osmotic conditions and hence cellular swelling occurs.

Morphological features:

Grossly, the affected organ is enlarged due to swelling.

Microscopically, it is characterized by:

- i. The cells are swollen and the microvasculature compressed.
- ii. Small clear vacuoles are seen in the cells.
- iii. Small cytoplasmic blebs may be seen.
- iv. The nucleus may appear pale.

2. Fatty change (steatosis): Fatty change, steatosis or fatty metamorphosis is the intracellular accumulation of neutral fat within parenchymal cells. The deposit is in the cytosol and represents an absolute increase in the intracellular lipids.

Fatty liver: Liver is the commonest site for accumulation of fat.

Etiology: Conditions with excess fat (hyperlipidemia), liver cell damage.

Pathogenesis: In fatty liver, intracellular accumulation of triglycerides can occur due to defect at one or more of the following 6 steps in the normal fat metabolism.

1. Increased entry of free fatty acids into the liver.
2. Increased synthesis of fatty acids by the liver.
3. Decreased conversion of fatty acids into ketone bodies.
4. Increased α -glycerophosphate causing increased esterification of fatty acids to triglycerides.
5. Decreased synthesis of 'lipid acceptor protein' resulting in decreased formation of lipoprotein from triglycerides.
6. Block in the excretion of lipoprotein from the liver into plasma.

Morphological features:

Grossly, the liver in fatty change is enlarged with a tense, glistening capsule and rounded margins.

Microscopically, characteristic feature is the presence of numerous lipid vacuoles in the cytoplasm of hepatocytes. Fat in H and E stained section prepared by paraffin embedding technique appear non-staining vacuoles because it is dissolved in alcohol.

3. Hyaline change: The word 'hyaline' means glassy. Hyaline is a descriptive histologic term for glassy, homogeneous, eosinophilic appearance of material in hematoxylin and eosin stained sections and does not refer to any specific substance. Hyaline change is associated with heterogeneous pathologic conditions. It may be intracellular or extracellular. Intracellular hyaline is mainly seen in epithelial cells. Examples are:

1. Hyaline degeneration of rectus abdominalis muscle called Zenker's degeneration, occurring in typhoid fever.
2. Mallory's hyaline in the hepatocytes in alcoholic liver cell injury.
3. Russell's bodies representing excessive immunoglobulins in the rough endoplasmic reticulum of the plasma cells.

Extracellular hyaline is seen in connective tissues. Examples are:

1. Hyaline degeneration in leiomyomas of the uterus.
2. Hyalinized old scar of fibrocollagenous tissues.

4. Muroid change: Mucin is normally produced by epithelial cells of mucous membranes and mucous glands as well as by some connective tissues like in the umbilical cord. By convention, connective tissue mucin is termed myxoid (mucus-like). Following are some examples of functional excess of epithelial mucin:

1. Catarrhal inflammation of mucous membrane.
2. Obstruction of duct leading to mucocoele in the oral cavity and gallbladder.
3. Cystic fibrosis of the pancreas.
4. Mucin-secreting tumors.

Examples of disturbances of connective tissue mucin are as under

1. Muroid or myxoid degeneration in some tumors, e.g. myxomas, neurofibromas, etc.
2. Dissecting aneurysm of the aorta due to Erdheim's medial degeneration and Marfan's syndrome.

Q. 8. Write a short note on melanin pigment.

(TNMGR, March 2009)

Q. Write a short note on endogenous pigments.

(TNMGR, April 2003)

Ans. Pigments are colored substances present in most living beings including humans.

a. Endogenous pigments: Endogenous pigments are either normal constituents of cells or accumulate under special circumstances, e.g. melanin, ochronosis, hemoprotein-derived pigments, and lipofuscin.

1. Melanin is the brown-black, non-hemoglobin-derived pigment normally present in the hair, skin, choroid of the eye, meninges and adrenal medulla. It is synthesized in the melanocytes and dendritic cells and stored in melanophores.

Disorders of melanin pigmentation

i. Generalized hyperpigmentation

- a. In Addison's disease.
- b. Chloasma.
- c. Chronic arsenical poisoning—raindrop pigmentation of the skin.

ii. Focal hyperpigmentation

- a. Cefé au lait spots—neurofibromatosis and Albright's syndrome.
- b. Peutz-Jeghers syndrome.
- c. Melanosis coli.
- d. Melanotic tumors.
- e. Lentigo.

iii. Generalized hypopigmentation: Albinism.

iv. Localized hypopigmentation

- a. Leukoderma
- b. Vitiligo
- c. Acquired focal hypopigmentation—leprosy, healing of wounds, radiation dermatitis, etc.

2. Melanin-like pigments containing diseases: Alkaptonuria, Dubin-Johnson syndrome.

3. Hemoprotein-derived pigments: Hemosiderin, hemozoin, bilirubin, and porphyrins.

4. Lipofuscin: Wear and tear pigment.

b. Exogenous pigments: Pigments introduced into the body from outside such as by inhalation, ingestion or inoculation.

1. Inhaled pigments: Carbon or coal dust; silica or stone dust, iron or iron oxide, asbestos and various other organic substances.

2. Ingested pigments

- i. Argyria is chronic ingestion of silver compounds and results in brownish pigmentation in the skin, bowel, and kidney.
- ii. Chronic lead poisoning may produce the characteristic blue lines on teeth at the gum line.
- iii. Carotenemia is yellowish-red coloration of the skin caused by excessive ingestion of carrots which contain carotene.

3. **Injected pigments (tattooing):** India ink, cinnabar and carbon.

Q. 9. Write a short note on metaplasia.

(TNMGR, April 2003)

Ans. Metaplasia is defined as a reversible change of one type of epithelial or mesenchymal adult cells to another type of adult epithelial or mesenchymal cells, usually in response to abnormal stimuli, and often reverts back to normal on removal of stimulus. However, if the stimulus persists for a long time, epithelial metaplasia may transform into cancer.

a. Epithelial metaplasia

1. **Squamous metaplasia:** This is more common, due to chronic irritation. For example:
 - i. In bronchus (normally lined by pseudostratified columnar ciliated epithelium) in chronic smokers.
 - ii. In vitamin A deficiency, apart from xerophthalmia, there is squamous metaplasia in the nose, bronchi, urinary tract, lacrimal and salivary glands.
2. **Columnar metaplasia:** There are some conditions in which there is transformation to columnar epithelium. For example:
 - i. Intestinal metaplasia in healed chronic gastric ulcer.
 - ii. Columnar metaplasia in Barrett's esophagus.

b. Mesenchymal metaplasia: For example:

1. **Osseous metaplasia:** Osseous metaplasia is formation of bone in fibrous tissue, cartilage and myxoid tissue.
 - i. In arterial wall in old age (Mönckeberg's medial calcific sclerosis).
 - ii. In scar of chronic inflammation of prolonged duration.
2. **Cartilaginous metaplasia:** In healing of fractures, cartilaginous metaplasia may occur where there is undue mobility.

Q. 10. Write a short note on pathologic calcification.

(TNMGR, Oct. 2003)

Ans. Deposition of calcium salts in tissues other than osteoid or enamel is called pathologic or heterotopic calcification. Two types:

i. Dystrophic calcification: Dystrophic calcification is characterized by deposition of calcium salts in dead or degenerated tissues with normal calcium metabolism and normal serum calcium levels.

a. Calcification in dead tissue:

1. Phlebolith.
2. Dead parasites in hydatid cyst, schistosoma eggs, and cysticercosis.

b. Calcification in degenerated tissues

1. Dense old scars.
2. Long standing cysts.

Pathogenesis: The denatured proteins in necrotic or degenerated tissue bind phosphate ions, which react with calcium ions to form precipitates of calcium phosphate.

ii. Metastatic calcification: Metastatic calcification occurs in apparently normal tissues and is associated with deranged calcium metabolism and hypercalcemia.

a. Excessive mobilization of calcium from the bone

1. Hyperparathyroidism.
2. Bony destructive lesions such as multiple myeloma, metastatic carcinoma.

b. Excessive absorption of calcium from the gut

1. Hypervitaminosis D.
2. Milk-alkali syndrome.

Pathogenesis: Metastatic calcification occurs due to excessive binding of inorganic phosphate ions with calcium ions, which are elevated due to underlying metabolic derangement. This leads to formation of precipitates of calcium phosphate at the preferential sites.

Q. 11. Write a short note on nerve injuries.

(BFUHS, May 2008)

Ans.

1. **Wallerian degeneration:** Following transection, there is accumulation of organelles in the proximal and distal ends of the transection sites. Subsequently, the axon and myelin sheath distal to the transection site undergo disintegration up to the next node of Ranvier, followed by phagocytosis. The process of regeneration occurs by sprouting of axons and proliferation of Schwann cells from the proximal end.

2. **Axonal degeneration:** In axonal degeneration, degeneration of the axon begins at the peripheral terminal and proceeds backward towards the nerve cell body. The cell body often undergoes chromatolysis. There is Schwann cell proliferation in the region of axonal degeneration.

3. **Segmental demyelination:** Segmental demyelination is loss of myelin of the segment between two consecutive nodes of Ranvier, leaving a denuded axon segment. The axon, however, remains intact. Repeated episodes of demyelination and remyelination are associated with concentric proliferation of Schwann cells around axons producing **onion bulbs** found in hypertrophic neuropathy.
4. **Traumatic neuroma:** Normally, the injured axon of a peripheral nerve regenerates at the rate of approximately 1 mm per day. However, if the process of regeneration is hampered due to an interposed hematoma or fibrous scar, the axonal sprouts together with Schwann cells and fibroblasts form a peripheral mass called as traumatic or stump neuroma.

3. NECROSIS AND GANGRENE

Q. 1. Define necrosis. Discuss in detail about the various types of necrosis.

(TNMGR, March 2008; KLE Uni. Jan. 2009; MUHS, May 2010; BFUHS, May 2011; RUHS, May 2015)

Ans. Necrosis is defined as a localized area of death of tissue followed by degradation of tissue by hydrolytic enzymes liberated from dead cells. It is characterized by:

- i. Cell digestion by lytic enzymes.
- ii. Denaturation of proteins.

Types

1. **Coagulative necrosis:** Most common type, caused by irreversible focal injury, mostly from ischemia, and less often from bacterial and chemical agents. The organs commonly affected are the heart, kidney, and spleen. Grossly, foci of coagulative necrosis in the early stage are pale, firm, and slightly swollen. With progression, they become more yellowish, softer, and shrunken. Microscopically, the hallmark of coagulative necrosis is the conversion of normal cells into their 'tombstones.' The necrosed cells are swollen and appear more eosinophilic than the normal. Cell digestion and liquefaction fail to occur. The necrosed focus is infiltrated by inflammatory cells and the dead cells are phagocytosed leaving granular debris and fragments of cells.
2. **Liquefaction (colliquative) necrosis:** It occurs due to degradation of tissue by the action of powerful hydrolytic enzymes. The common examples are infarct brain and abscess cavity. Grossly, the affected area is soft with liquefied center containing necrotic debris. Later, a cyst wall is formed. Microscopically, the cystic space contains necrotic cell debris and

macrophages filled with phagocytosed material. The cyst wall is formed by proliferating capillaries, inflammatory cells and proliferating glial cells in the case of brain and proliferating fibroblasts in the case of abscess cavity.

3. **Caseous necrosis:** Caseous necrosis is found in the centre of foci of tuberculous infections. It combines features of both coagulative and liquefactive necrosis. Grossly, foci of caseous necrosis resemble dry cheese and are soft, granular and yellowish. Microscopically, the necrosed foci are structureless, eosinophilic, and contain granular debris. The surrounding tissue shows characteristic granulomatous inflammatory reaction.
4. **Fat necrosis:** Fat necrosis is a special form of cell death occurring at two anatomically different locations but morphologically similar lesions. These are: following acute pancreatic necrosis, and traumatic fat necrosis commonly in breasts.

In the case of pancreas, there is liberation of pancreatic lipases from injured or inflamed tissue that results in necrosis of the pancreas as well as of the fat depots throughout the peritoneal cavity. Fat necrosis hydrolyses neutral fat present in adipose cells into glycerol and free fatty acids. The damaged adipose cells assume cloudy appearance. The leaked out free fatty acids complex with calcium to form calcium soaps (**saponification**).

Grossly, fat necrosis appears as yellowish-white and firm deposits. Formation of calcium soaps imparts the necrosed foci firmer and chalky white appearance.

Microscopically, the necrosed fat cells have cloudy appearance and are surrounded by an inflammatory reaction. Formation of calcium soaps is identified in the tissue sections as amorphous, granular and basophilic material.

5. **Fibrinoid necrosis:** Fibrinoid necrosis is characterized by deposition of fibrin-like material which has the staining properties of fibrin. It is encountered in various immunologic tissue injuries (e.g. immune complex vasculitis, autoimmune diseases, Arthus reaction, etc.), arterioles in hypertension, peptic ulcer, etc. Microscopically, fibrinoid necrosis is identified by brightly eosinophilic, hyaline-like deposition in the vessel wall. Necrotic focus is surrounded by nuclear debris of neutrophils (leukocytoclasia).

Q. 2. Write about gangrene. (TNMGR, March 2007)

Ans. Gangrene is a form of necrosis of tissue with superadded putrefaction. The type of necrosis is usually coagulative due to ischemia.

1. **Dry gangrene:** Causes are ischemia, thromboangiitis obliterans (Buerger's disease), Raynaud's disease, trauma, and ergot poisoning. It is usually initiated in one of the toes which is farthest from the blood supply, and then spreads slowly upwards until it reaches a point where the blood supply is adequate to keep the tissue viable. The affected part is dry, shrunken and dark black, resembling the foot of a mummy. The line of separation usually brings about complete separation with eventual falling off of the gangrenous tissue if it is not removed surgically. Histologically, there is necrosis with smudging of the tissue.
2. **Wet gangrene:** Wet gangrene occurs in naturally moist tissues and organs such as the mouth. Diabetic foot, bed sores are example of wet gangrene. Wet gangrene usually develops rapidly due to blockage of venous and less commonly, arterial blood flow from thrombosis or embolism. The affected part is stuffed with blood which favors the rapid growth of putrefactive bacteria. The toxic products formed by bacteria are absorbed causing profound systemic manifestations of septicemia and finally death. Grossly, the affected part is soft, swollen, putrid, rotten and dark. Histologically, there is coagulative necrosis with stuffing of affected part with blood.
3. **Gas gangrene:** It is a special form of wet gangrene caused by gas-forming clostridia (gram-positive anaerobic bacteria) which gain entry into the tissues through open contaminated wounds, especially in the muscles, or as a complication of operation on colon which normally contains clostridia. Clostridia produce various toxins which produce necrosis and edema locally and are also absorbed producing profound systemic manifestations. Grossly, the affected area is swollen, edematous, painful and crepitant due to accumulation of gas bubbles within the tissues. Subsequently, the affected tissue becomes dark black and foul smelling. Microscopically, the muscle fibres undergo coagulative necrosis with liquefaction.

Q. 3. Write a short note on apoptosis.

(TNMGR, March 2008; RUHS, May 2015)

Ans. Apoptosis is a form of 'coordinated and internally programmed cell death.'

Physiologic processes

1. Organized cell destruction during development of embryo.
2. Physiologic involution of cells in hormone-dependent tissues, e.g. endometrial shedding, regression of lactating breast after withdrawal of breastfeeding.

3. Normal cell destruction followed by replacement proliferation such as in intestinal epithelium.
4. Involution of the thymus in early age.

Pathologic processes

1. Cell death in tumors exposed to chemotherapeutic agents.
2. Cell death by cytotoxic T cells in immune mechanisms such as in graft-versus-host disease and rejection reactions.
3. Progressive depletion of CD4+ T cells in the pathogenesis of AIDS.
4. Cell death in viral infections, e.g. formation of Councilman bodies in viral hepatitis.

Characteristic morphologic changes

1. Involvement of single cells or small clusters of cells in the background of viable cells.
2. The apoptotic cells are round to oval shrunken masses of intensely eosinophilic cytoplasm (mummified cell) containing shrunken or almost-normal organelles.
3. The nuclear chromatin is condensed or fragmented (**pyknosis or karyorrhexis**).
4. The cell membrane may show convolutions or projections on the surface.
5. There may be formation of membrane-bound near spherical bodies on or around the cell called apoptotic bodies containing compacted organelles.
6. Characteristically, there is no acute inflammatory reaction around apoptosis.
7. Phagocytosis of apoptotic bodies by macrophages takes place at varying speed.

Apoptotic cells can be identified and counted by following methods

1. Staining of chromatin condensation (hematoxylin, Feulgen, acridine orange).
2. Flow cytometry.
3. DNA changes detected by *in situ* techniques or by gel electrophoresis.
4. Annexin V as marker for apoptotic cell membrane.

Molecular mechanisms of apoptosis

1. **Initiators of apoptosis**
 - i. Withdrawal of signals required for normal cell survival.
 - ii. Extracellular signals triggering of programmed cell death.
 - iii. Intracellular stimuli, e.g. heat, radiation, hypoxia, etc.
2. **Process of programmed cell death**
 - i. Activation of caspases.
 - ii. Activation of death receptors.

- iii. Activation of growth controlling genes (BCL-2 and p53).
 - iv. Cell death.
3. **Phagocytosis:** The dead apoptotic cells develop membrane changes which promote their phagocytosis.

4. CIRCULATORY DISTURBANCES

Q. 1. Write a short note on shock and its types.

(BFUHS, May 2004; TNMGR, Aug. 2004, March 2010)

Q. Describe the pathophysiology of shock.

(TNMGR, March 2007, April 2012; RGUHS, Nov. 2011)

Ans. Shock is defined as an acute reduction of effective circulating blood volume (hypotension); and an inadequate perfusion of cells and tissues (hypoperfusion) (see table below).

Classification and Etiology

1. Hypovolemic shock

- i. Acute hemorrhage.
- ii. Dehydration from vomiting, diarrhea.
- iii. Burns.
- iv. Excessive use of diuretics.
- v. Acute pancreatitis.

2. Cardiogenic shock

- i. Deficient emptying, e.g. myocardial infarction, cardiomyopathies and cardiac arrhythmias.

- ii. Deficient filling, e.g. cardiac tamponade from hemopericardium.
- iii. Obstruction to the outflow, e.g. pulmonary embolism, dissecting aortic aneurysm.

3. Septic shock

- i. Gram-negative septicemia (**endotoxic shock**), e.g. infection with *E. coli*, *Proteus*, *Klebsiella*, *Pseudomonas* and *Bacteroides*.
- ii. Gram-positive septicemia (**exotoxic shock**), e.g. infection with streptococci, pneumococci.

4. Other types

- i. **Traumatic shock:** Severe injuries, surgery with marked blood loss.
- ii. **Neurogenic shock:** High cervical spinal cord injury, high spinal anesthesia, head injury.
- iii. **Hypoadrenal shock:** Administration of high doses of glucocorticoids, secondary adrenal insufficiency.

Pathogenesis

1. **Reduced effective circulating blood volume:** It may result by either of the following mechanisms:

- i. By actual loss of blood volume as occurs in hypovolemic shock.
- ii. By decreased cardiac output without actual loss of blood (normovolemia) as occurs in cardiogenic shock and septic shock.

2. **Impaired tissue oxygenation:** Following reduction in the effective circulating blood volume, there is decreased venous return to the heart resulting in decreased cardiac output. This consequently causes reduced supply of oxygen to the organs and tissues and hence tissue anoxia, which sets in cellular injury.

3. **Release of inflammatory mediators:** In response to cellular injury, innate immunity of the body gets activated and release inflammatory mediators. Endotoxins in bacterial wall in septic shock stimulate massive release of pro-inflammatory mediators (cytokines). The most important being the tumor necrosis factor α (TNF- α) and interleukin-1 (IL-1) cytokines.

Q. 2. Write a short note on causes of edema.

(TNMGR, April 1998, Oct. 2000)

Q. Discuss the pathogenesis of edema.

(TNMGR, Aug. 2004)

Ans. Edema may be defined as abnormal and excessive accumulation of "free fluid" in the interstitial tissue spaces and serous cavities. The edema may be of 2 main types (see table on next page):

1. **Localized:** When limited to an organ or limb, e.g. lymphatic edema, inflammatory edema, allergic edema.

Stages of shock	Pathogenesis	Effects
Compensated shock (initial)	<ul style="list-style-type: none"> i. Widespread vasoconstriction ii. Fluid conservation by kidney iii. Stimulation of adrenal medulla 	<ul style="list-style-type: none"> i. Tachycardia ii. Cool, clammy skin
Progressive decompensated shock	<ul style="list-style-type: none"> i. Pulmonary hypoperfusion ii. Tissue ischemia 	<ul style="list-style-type: none"> i. ↓ Cardiac output ii. Mental confusion iii. ↓ Urinary output iv. Tachypnea
Irreversible decompensated shock	<ul style="list-style-type: none"> i. Progressive vasodilation ii. ↑ Vascular permeability iii. Myocardial depressant factor iv. Pulmonary hypoperfusion v. Anoxic damage vi. Hypercoagulability 	<ul style="list-style-type: none"> i. <i>Brain:</i> hypoxic encephalopathy ii. <i>Heart:</i> Focal myocardial necrosis iii. <i>Lungs:</i> ARDS (adult respiratory distress syndrome) iv. <i>Adrenals:</i> Necrosis v. <i>GIT:</i> Hemorrhagic gastroenteropathy vi. <i>Liver:</i> Necrosis vii. <i>Blood:</i> DIC

Feature	Transudate	Exudate
Definition	Filtrate of blood plasma without changes in endothelial permeability	Edema of inflamed tissue associated with increased vascular permeability
Character	Non-inflammatory edema	Inflammatory edema
Protein content	Low	High
Glucose content	Same as in plasma	Low
Specific gravity	Less than 1.015	More than 1.018
pH	>7.3	<7.3
LDH	Low	High
Cells	Few cells, mainly mesothelial and cellular debris	Many cells, inflammatory as well parenchymal

2. **Generalized (anasarca or dropsy):** When it is systemic in distribution, particularly noticeable in the subcutaneous tissues, e.g. renal edema, cardiac edema, nutritional edema.

Depending upon fluid composition, edema fluid may be **Transudate** which is more often the case, such as in edema of cardiac and renal disease; or **Exudate** such as in inflammatory edema.

Pathogenesis of edema

1. Decreased plasma oncotic pressure.
2. Increased capillary hydrostatic pressure.
3. Lymphatic obstruction.
4. Tissue factors (increased oncotic pressure of interstitial fluid, and decreased tissue tension).
5. Increased capillary permeability.
6. Sodium and water retention.

Q. 3. Describe the mechanism of thrombus formation.
(TNMGR, Oct. 1999)

Q. Define thrombosis. Discuss the pathogenesis of thrombosis formation.
(TNMGR, April 2001)

Q. Write a short note on Virchow's triad.
(TNMGR, March 2007)

Ans. Thrombosis is the process of formation of solid mass in circulation from the constituents of flowing blood; the mass itself is called a **thrombus**. In contrast, a **blood clot** is the mass of coagulated blood formed *in vitro*, e.g. in a test tube. **Hematoma** is the extravascular accumulation of blood clot, e.g. into the tissues. **Hemostatic plugs** are the blood clots formed in healthy

individuals at the site of bleeding, e.g. in injury to the blood vessel. Thrombi may be life-threatening by causing one of the following harmful effects:

1. Ischemic injury
2. Thromboembolism

Pathophysiology: Virchow described three primary events which predispose to thrombus formation (**Virchow's triad**)—endothelial injury, altered blood flow, and hypercoagulability of blood. To this are added the processes that follow these primary events: Activation of platelets and of clotting system. These events are discussed below:

1. **Endothelial injury:** Vascular injury exposes the subendothelial connective tissue (thrombogenic) and also causes vasoconstriction of small blood vessels briefly so as to reduce the blood loss.
2. **Role of platelets:** Following endothelial cell injury, the sequence of events is:
 - i. **Platelet adhesion:** The platelets in circulation recognize the site of endothelial injury and with the help of von Willebrand's factor, adhere to exposed subendothelial collagen (**primary aggregation**).
 - ii. **Platelet release reaction**
 - a. **Alpha granules:** Fibrinogen, fibronectin, platelet derived growth factor, platelet factor 4.
 - b. **Dense bodies:** ADP (adenosine diphosphate), ionic calcium, 5-HT (serotonin), histamine and epinephrine.
 - iii. **Platelet aggregation:** Following release of ADP, aggregation of additional platelets takes place (**secondary aggregation**). This results in formation of temporary hemostatic plug.
3. **Role of coagulation system**
 - i. **In the intrinsic pathway:** **Contact** with abnormal surface leads to activation of factor XII and the sequential interactions of factors XI, IX, VIII and finally factor X, along with calcium ions (factor IV) and platelet factor 3.
 - ii. **In the extrinsic pathway:** **Tissue damage** results in the release of tissue factor or thromboplastin. Tissue factor on interaction with factor VII activates factor X.
 - iii. **The common pathway:** Where both intrinsic and extrinsic pathways converge to activate factor X which forms a complex with factor Va and platelet factor 3, in the presence of calcium ions. This complex activates prothrombin (factor II) to thrombin (factor IIa) which, in turn, converts fibrinogen to fibrin. Initial monomeric fibrin is polymerized to form insoluble fibrin by activation of factor XIII.

Regulation of coagulation system: The blood is kept in fluid state normally and coagulation system kept in check by controlling mechanisms. These are as under:

- a. Protease inhibitors oppose the formation of thrombin, e.g. antithrombin III, protein C, C1 inactivator, α 1-antitrypsin, α 2-macroglobulin.
 - b. **Fibrinolytic system:** Plasmin acts on fibrin to destroy the clot.
- 4. Alteration of blood flow:** Turbulence and stasis occur in thrombosis in which the normal axial flow of blood is disturbed. Formation of arterial and cardiac thrombi is facilitated by turbulence in the blood flow, while stasis initiates the venous thrombi even without evidence of endothelial injury.
- 5. Hypercoagulability of blood:** Hypercoagulability may occur by the following changes in the composition of blood:
- i. Increase in coagulation factors, e.g. fibrinogen, prothrombin, factors VIIa, VIIIa and Xa.
 - ii. Increase in platelet count and their adhesiveness.
 - iii. Decreased levels of coagulation inhibitors, e.g. antithrombin III, fibrin split products.

Predisposing factors

Primary (genetic) factors

- i. Deficiency of antithrombin
- ii. Deficiency of protein C or S
- iii. Defects in fibrinolysis
- iv. Mutation in factor V

Secondary (acquired) factors

- a. Risk factors:
 - i. Advanced age
 - ii. Prolonged bedrest
 - iii. Immobilization
 - iv. Cigarette smoking
- b. Clinical conditions predisposing to thrombosis:
 - i. Heart diseases
 - ii. Vascular diseases
 - iii. Hypercoagulable conditions
 - iv. Shock

Morphologic features: Thrombosis may occur in the heart, arteries, veins and the capillaries. Arterial thrombi produce ischemia and infarction, whereas cardiac and venous thrombi cause embolism. Grossly, thrombi may be of various shapes, sizes and composition depending upon the site of origin. Arterial thrombi tend to be white and mural while the venous thrombi are red and occlusive. Mixed or laminated thrombi are consisting of alternate white and red layers

called **lines of Zahn**. Red thrombi are soft, red and gelatinous whereas white thrombi are firm and pale.

Microscopically, the composition of thrombus is determined by the rate of flow of blood, i.e. whether it is formed in the rapid arterial and cardiac circulation, or in the slow moving flow in veins.

Fate of Thrombus

1. Resolution
2. Organization
3. Propagation
4. Thromboembolism

Clinical Effects

1. **Cardiac thrombi:** Sudden death by mechanical obstruction of blood flow or through thromboembolism to vital organs.
2. **Arterial thrombi:** Sudden death may occur following thrombosis of coronary artery.
3. **Venous thrombi (phlebothrombosis):** These may cause following effects:
 - i. Thromboembolism
 - ii. Edema of area drained
 - iii. Poor wound healing
 - iv. Skin ulcer
 - v. Painful thrombosed veins (thrombophlebitis)
 - vi. Painful white leg (**phlegmasia alba dolens**) due to iliofemoral venous thrombosis in postpartum cases
4. **Capillary thrombi:** Disseminated intravascular coagulation (DIC).

Q. 4. Define and classify embolus.

(TNMGR, March 2002; RGUHS, Oct. 2010)

Q. Write a short note on fat embolism.

(TNMGR, Nov. 2001)

Ans. Embolism is the process of partial or complete obstruction of some part of the cardiovascular system by any mass carried in the circulation; the transported intravascular mass detached from its site of origin is called an **embolus**. Most usual forms of emboli (90%) are thromboemboli.

a. Depending upon the matter in the emboli

- i. Solid, e.g. thromboemboli, atheromatous material, tumor cell clumps, tissue fragments, parasites, bacterial clumps, foreign bodies.
- ii. Liquid, e.g. fat globules, amniotic fluid, bone marrow.
- iii. Gaseous, e.g. air, other gases.

b. Depending upon whether infected or not

- i. Bland—sterile
- ii. Septic—infected

c. Depending upon the source of the emboli

- i. Cardiac emboli from left side of the heart, e.g. emboli originating from atrium and atrial appendages, infarct in the left ventricle.
- ii. Arterial emboli, e.g. in systemic arteries in the brain, spleen, kidney, intestine.
- iii. Venous emboli, e.g. in pulmonary arteries.
- iv. Lymphatic emboli.

d. Depending upon the flow of blood

- i. Paradoxical embolus.
- ii. Retrograde embolus.

Thromboembolism: A detached thrombus or part of thrombus constitutes the most common type of embolism. These may arise in the arterial or venous circulation:

1. **Arterial (systemic) thromboembolism:** Arterial emboli may be derived from within the heart (80–85%), or from within the arteries.
2. **Venous thromboembolism:** Thrombi in the veins of the lower legs—most common cause. It leads to pulmonary embolism—pulmonary embolism is the most common and fatal form of venous thromboembolism in which there is occlusion of pulmonary arterial tree by thromboemboli. Consequences: Sudden death, acute cor pulmonale, pulmonary infarction, pulmonary hemorrhage, resolution, pulmonary hypertension, chronic cor pulmonale and pulmonary arteriosclerosis.
3. **Systemic embolism:** This is the type of arterial embolism that originates commonly from thrombi in the diseased heart, especially in the left ventricle. These arterial emboli invariably cause infarction at the sites of lodgment. The effects and sites of arterial emboli are in striking contrast to venous emboli which are often lodged in the lungs.
4. **Fat embolism:** Obstruction of arterioles and capillaries by fat globules constitutes fat embolism. If the obstruction in the circulation is by fragments of adipose tissue, it is called fat-tissue embolism.

Etiology

- i. Trauma to bones is the most common cause of fat embolism.
- ii. **Non-traumatic causes:** Burns, diabetes mellitus, fatty liver, sickle cell anemia.

Pathogenesis

- i. **Mechanical theory:** Trauma leads to release of fat globules into the circulation.
- ii. **Emulsion instability theory:** Fat emboli are formed by aggregation of plasma lipids (chylomicrons and fatty acids).
- iii. **Intravascular coagulation theory:** Activation of DIC.
- iv. **Toxic injury theory:** High plasma levels of free fatty acid causes toxic injury.

Consequences

- i. Pulmonary fat embolism.
- ii. Systemic fat embolism.
 - a. Brain—petechial hemorrhages.
 - b. Kidney—tubular damage and renal insufficiency.
- 5. **Gas embolism:** Air, nitrogen and other gases can produce bubbles within the circulation and obstruct the blood vessels causing damage to tissue. Two main forms of gas embolism—air embolism and decompression sickness.

5. NEOPLASM

Q. 1. Define neoplasia. How does benign neoplasia differ from malignant neoplasia? Discuss in detail the various carcinogens with special reference to oral carcinoma.

(Bangalore Uni., Jan. 1992; TNMGR, Sept. 2010)

Q. Discuss the spread of malignant tumors and metastasis.

(BFUHS, May 2008; TNMGR, March 2007, 2008; April 2013)

Q. Write about the morphology of malignant cell.

(TNMGR, Nov. 1995)

Ans. Neoplasia means “new growth,” and a new growth is called a neoplasm. The eminent British oncologist Willis defined: “A neoplasm is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change.”

All tumors have two basic components: (i) neoplastic cells that constitute the tumor parenchyma and (ii) reactive stroma made up of connective tissue, blood vessels, and variable numbers of cells of the adaptive and innate immune system.

Benign tumors: A tumor is said to be benign when its gross and microscopic appearances are considered relatively innocent, implying that it will remain localized,

will not spread to other sites, and is amenable to local surgical removal. In general, benign tumors are designated by attaching the suffix—oma to the name of the cell type from which the tumor originates.

Malignant tumors: Malignant tumors are collectively referred to as cancers. Malignant tumors can invade and destroy adjacent structures and spread to distant sites (metastasize) to cause death. Malignant tumors arising in solid mesenchymal tissues are usually called **sarcomas** whereas those arising from blood-forming cells are designated **leukemias** or **lymphomas**. Malignant neoplasms of epithelial cell origin are called **carcinomas**.

Mixed tumors: When two types of tumors are combined in the same tumor, it is called a mixed tumor.

Teratomas: These tumors are made up of a mixture of various tissue types arising from totipotent cells derived from the three germ cell layers—ectoderm, mesoderm and endoderm.

Blastomas (embryomas): Blastomas or embryomas are a group of malignant tumors which arise from embryonal or partially differentiated cells which would normally form blastoma of the organs and tissue during embryogenesis.

Hamartoma: It is benign tumor which is made of mature but disorganized cells of tissues indigenous to the particular organ.

Choristoma: It is the name given to the ectopic islands of normal tissue. Thus, choristoma is heterotopia but is not a true tumor.

Characteristics of Tumors

1. Differentiation and anaplasia

Differentiation: The extent to which neoplastic parenchymal cells resemble the corresponding normal parenchymal cells, both morphologically and functionally.

Anaplasia: Lack of differentiation is called anaplasia.

In general, benign tumors are well differentiated. In well-differentiated benign tumors, mitoses are usually rare and are of normal configuration. In contrast, while malignant neoplasms exhibit a wide range of parenchymal cell differentiation, most exhibit morphologic alterations that betray their malignant nature. Malignant neoplasm that are composed of poorly differentiated cells are said to be **anaplastic**. Lack of differentiation, or anaplasia, is considered a **hallmark of malignancy**. Anaplasia, is often associated with many other morphologic changes.

- a. **Pleomorphism:** Cancer cells often display pleomorphism (variation in size and shape).
- b. **Abnormal nuclear morphology:** Characteristically, the nuclei are disproportionately large for the cell, with a nuclear-to-cytoplasm ratio (N : C) that may approach 1 : 1 instead of the **normal 1 : 4 or 1 : 6**. The nuclear shape is variable and often irregular, and the chromatin is often coarsely clumped and distributed along the nuclear membrane, or more darkly stained than normal (**hyperchromatic**). Abnormally large nucleoli are also commonly seen.
- c. **Mitoses:** In undifferentiated tumors, many cells are in mitosis, reflecting the high proliferative activity of the parenchymal cells. The presence of mitoses, however, does not necessarily indicate that a tumor is malignant. More important as a morphologic feature of malignancy are atypical, bizarre mitotic figures, sometimes with tripolar, quadripolar, or multipolar spindles.
- d. **Loss of polarity:** The orientation of anaplastic cells is markedly disturbed. Sheets or large masses of tumor cells grow in an anarchic, disorganized fashion.
- e. **Other changes:** In many rapidly growing malignant tumors develop large central areas of ischemic necrosis.

2. Metaplasia and dysplasia

Metaplasia is defined as the replacement of one type of cell with another type. Metaplasia is nearly always found in association with tissue damage, repair, and regeneration, e.g. gastroesophageal reflux damages the squamous epithelium of the esophagus, leading to its replacement by glandular (gastric or intestinal) epithelium more suited to an acidic environment.

Dysplasia: It is a term that literally means “disordered growth.” It is encountered principally in epithelia and is characterized by a constellation of changes that include a loss in the uniformity of the individual cells as well as a loss in their architectural orientation. For example in dysplastic squamous epithelium the normal progressive maturation of tall cells in the basal layer to flattened squames on the surface may fail in part or entirely, leading to replacement of the epithelium by basal-appearing cells with hyperchromatic nuclei. In addition, mitotic figures are more abundant than in the normal tissue and may be seen at all levels, including surface cells. When dysplastic changes are marked and involve the full thickness of the epithelium, but the lesion does not penetrate the basement membrane, it is referred to as **carcinoma in situ**. Once the tumor cells breach the basement membrane, the tumor is said to be **invasive**.

Local invasion: The growth of cancers is accompanied by progressive infiltration, invasion, and destruction of the surrounding tissue, whereas nearly all benign tumors grow as cohesive expansile masses that remain localized to their site of origin and lack the capacity to infiltrate, invade, or metastasize to distant sites. In contrast, malignant tumors are, poorly demarcated from the surrounding normal tissue, and a well-defined cleavage plane is lacking. Histologic examination of such "pseudo-encapsulated" masses almost always shows rows of cells penetrating the margin and infiltrating the adjacent structures, a crab-like pattern of growth that constitutes the popular image of cancer. Next to the development of metastases, invasiveness is the most reliable feature that differentiates cancers from benign tumors.

3. Metastases

It is defined by the spread of a tumor to sites, those are physically discontinuous with the primary tumor. All malignant tumors can metastasize (exception—gliomas and basal cell carcinomas of the skin). In general, the likelihood of a primary tumor metastasizing correlates with lack of differentiation, aggressive local invasion, rapid growth, and large size. Metastatic spread strongly reduces the possibility of cure.

Pathways of Spread (Spread of Tumor)

- i. **Seeding of body cavities and surfaces:** It may occur whenever a malignant neoplasm penetrates into a natural "open field" lacking physical barriers. Most often involved is the peritoneal cavity, but any other cavity—pleural, pericardial, subarachnoid, and joint spaces may be affected. Such seeding is particularly characteristic of carcinomas arising in the ovaries, which spread to peritoneal surfaces, which become coated with a heavy cancerous glaze.
- ii. **Lymphatic spread:** Transport through lymphatics is the most common pathway for the initial dissemination of carcinomas. Sarcomas may also use this route. The pattern of lymph node involvement follows the natural routes of lymphatic drainage. Generally, regional lymph nodes draining the tumor are invariably involved producing regional nodal metastasis. Local lymph nodes may be bypassed so-called **skip metastasis** because of venous-lymphatic anastomoses or because inflammation or radiation has obliterated lymphatic channels. Due to obstruction of the lymphatics by tumor cells, the lymph flow is disturbed and tumor cells spread against the flow of lymph causing retrograde metastases at unusual

sites. Virchow's lymph node is nodal metastasis preferentially to supraclavicular lymph node from cancers of abdominal organs, e.g. cancer stomach, colon, and gallbladder. Biopsy of sentinel nodes is often used to assess the presence or absence of metastatic lesions in the lymph nodes (sentinel lymph node—the first node in a regional lymphatic basin that receives lymph flow from the primary tumor). Enlargement of nodes may be caused by the spread and growth of cancer cells or reactive hyperplasia.

- iii. **Hematogenous spread:** Hematogenous spread is typical of sarcomas but is also seen with carcinomas. The liver and the lungs are most frequently involved in such hematogenous dissemination, because all portal area drainage flows to the liver and all caval blood flows to the lungs.

Benign and malignant tumors can be distinguished on the basis of a number of histologic and anatomic features (see table on next page).

Q. 2. Write a short note on carcinogenesis.

(TNMGR, March 2010; RGUHS, Oct. 2010)

Q. Write a short note on carcinogenic viruses.

(TNMGR, April 2012)

Q. Write about carcinogens.

(Nagpur Uni., Oct. 2004; TNMGR, Sept. 2009)

Q. List the steps from tumor inception to macro-metastases.

(TNMGR, 2011)

Ans. Carcinogenesis or oncogenesis or tumorigenesis means mechanism of induction of tumors agents which can induce tumors are called carcinogens. The etiology and pathogenesis of cancer include.

A. Molecular Pathogenesis of Cancer (Genetic Mechanisms of Cancer)

The general concept of molecular mechanisms of cancer:

1. **Monoclonality of tumors:** There is strong evidence to support that most human cancers arise from a single clone of cells by genetic transformation or mutation. For example in a case of multiple myeloma there is production of a single type of immunoglobulin or its chain as seen by monoclonal spike in serum electrophoresis.
2. **Field theory of cancer:** In an organ developing cancer, limited number of cells only grows into cancer after undergoing sequence of changes under the influence of etiologic agents. This is termed as 'field effect' and the concept called as field theory of cancer.

Features	Benign	Malignant
I. Clinical and gross features		
Boundaries	Well-circumscribed	Poorly circumscribed
Surrounding tissue	Often compressed	Usually invaded
Size	Usually small	Often larger
Secondary changes	Less often	More often
II. Microscopic features		
Pattern	Usually resembles the tissue of origin closely	Poor resemblance to tissue of origin
Basal polarity	Retained	Often lost
Pleomorphism	Usually not present	Often present
Nucleo-cytoplasmic ratio	Normal	Increased
Anisonucleosis	Absent	Present
Hyperchromatism	Absent	Present
Mitoses	May be present but are always typical mitoses	Increased mitotic figure, atypical and abnormal
Tumor giant cells	May be present but without nuclear atypia	Present with nuclear atypia
Chromosomal abnormalities	Infrequent	Present
Function	Usually well maintained	May be retained, lost or become abnormal
III. Growth rate	Usually slow	Usually rapid
IV. Local invasion	Often compresses the surrounding tissues without invading or infiltrating them	Infiltrates and invades the adjacent tissues
V. Metastasis	Absent	Present
VI. Prognosis	Local complications	Death by local and metastatic complications

3. Multi-step process of cancer growth and progression: Carcinogenesis is a gradual multistep process involving many generations of cells. The various causes may act on the cell one after another (multi-hit process). The same process is also involved in further progression of the tumor. Ultimately, the cells so formed are genetically and phenotypically transformed cells having phenotypic features of malignancy—excessive growth, invasiveness and distant metastasis.

4. Genetic theory of cancer: In cancer, there are either genetic abnormalities in the cell, or there are normal genes with abnormal expression. The abnormalities in genetic composition may be from inherited or induced mutations. The mutated cells transmit their characters to the next progeny of cells and result in cancer.

5. Genetic regulators of normal and abnormal mitosis: In normal cell growth, there are 4 regulatory genes:

- Proto-oncogenes are growth-promoting genes, i.e. they encode for cell proliferation pathway.
- Anti-oncogenes are growth-inhibiting or growth suppressor genes.
- Apoptosis regulatory genes control the programmed cell death.
- DNA repair genes are those normal genes which regulate the repair of DNA damage that has occurred during mitosis and also control the damage to proto-oncogenes and antioncogenes.

In cancer, the transformed cells are produced by abnormal cell growth due to genetic damage to these normal controlling genes. Thus, corresponding abnormalities in these 4 cell regulatory genes are as under:

- Activation of growth-promoting oncogenes causing transformation of cell. Mutant form of normal proto-oncogene in cancer is termed oncogene.
- Inactivation of cancer-suppressor genes.
- Abnormal apoptosis regulatory genes which may act as oncogenes or anti-oncogenes.
- Failure of DNA repair genes and thus inability to repair the DNA damage resulting in mutations.

Cancer-related genes and cell growth (hallmarks of cancer)

- Excessive and autonomous growth:** Growth-promoting oncogenes.
- Refractoriness to growth inhibition:** Growth suppressing anti-oncogenes.
- Escaping cell death by apoptosis:** Genes regulating apoptosis and cancer.
- Avoiding cellular aging:** Telomeres and telomerase in cancer.
- Continued perfusion of cancer:** Cancer angiogenesis.
- Invasion and distant metastasis:** Cancer dissemination.
- DNA damage and repair system:** Mutator genes and cancer.
- Cancer progression and tumor heterogeneity:** Clonal aggressiveness.

9. *Cancer, a sequential multistep molecular phenomenon: Multistep theory.*
10. *MicroRNAs in cancer: OncomiRs.*

B. Chemical Carcinogenesis

Stages in chemical carcinogenesis: Basic mechanism of chemical carcinogenesis is by induction of mutation in the proto-oncogenes and anti-oncogenes. The phenomena of cellular transformation by chemical carcinogens (as also other carcinogens) is a progressive process involving 3 sequential stages:

1. Initiation of carcinogenesis: Initiation is the first stage in carcinogenesis induced by initiator chemical carcinogens. The change so induced is sudden, irreversible and permanent. In either case, the following steps are involved in transforming 'the target cell' into 'the initiated cell':

- a. *Metabolic activation:* The indirect-acting carcinogens are activated in the liver by the mono-oxygenases of the cytochrome P450 system in the endoplasmic reticulum.
 - b. *Reactive electrophiles:* While direct-acting carcinogens are intrinsically electrophilic, indirect-acting substances become electron-deficient after metabolic activation, i.e. they become reactive electrophiles, which binds to DNA, RNA and other proteins.
 - c. *Target molecules:* The primary target of electrophiles is DNA, producing mutagenesis.
 - d. *The initiated cell:* The unrepaired damage produced in the DNA of the cell becomes permanent and fixed only if the altered cell undergoes at least one cycle of proliferation. This results in transferring the change to the next progeny of cells so that the DNA damage becomes permanent and irreversible.
- 2. Promotion of carcinogenesis:** Promoters of carcinogenesis are substances such as phorbol esters, phenols, hormones, artificial sweeteners and drugs like phenobarbital.
- 3. Progression of carcinogenesis:** Progression of cancer is the stage when mutated proliferated cell shows phenotypic features of malignancy. Such phenotypic features appear only when the initiated cell starts to proliferate rapidly and in the process acquires more and more mutations.

Carcinogenic Chemicals in Humans

- 1. Initiator carcinogens:** Chemical carcinogens which can initiate the process of neoplastic transformation are further categorized into 2 subgroups:
 - i. *Direct acting carcinogens:* These chemical carcinogens do not require metabolic activation and fall into 2 classes:
 - a. *Alkylating agents:* This group includes mainly various anti-cancer drugs (e.g. cyclophosphamide, chlorambucil, busulfan, melphalan, nitrosourea, etc). They are weakly carcinogenic and are implicated in the etiology of the lymphomas and leukemias in human beings.
 - b. *Acylating agents:* The examples are acetyl imidazole and dimethyl carbamyl chloride.
 - ii. *Indirect acting carcinogens (pro-carcinogens):* These are chemical substances which require prior metabolic activation before becoming potent 'ultimate' carcinogens. It includes the following 4 categories:
 - a. *Polycyclic aromatic hydrocarbons:* Combustion and chewing of tobacco, smoke, fossil fuel (e.g. coal), soot, tar, mineral oil, smoked animal foods, industrial and atmospheric pollutants.
 - b. *Aromatic amines and azo-dyes:* β -naphthylamine, aniline dye and rubber industry workers, Benzidine, Azo-dyes used for coloring foods.
 - c. *Naturally occurring products:* Aflatoxin B₁, actinomycin D, mitomycin C, safrole and betel nuts.
 - d. *Miscellaneous:* Nitrosamines and nitrosamides, vinyl chloride monomer, asbestos, metals like nickel, lead, cobalt, chromium, insecticides and fungicides.

2. Promoter carcinogens: Promoters are chemical substances which lack the intrinsic carcinogenic potential but their application subsequent to initiator exposure helps the initiated cell to proliferate further. These substances include phorbol esters, phenols, certain hormones and drugs.

C. Physical Carcinogenesis

Physical agents in carcinogenesis are divided into 2 groups:

- 1. Radiation carcinogenesis:** Ultraviolet (UV) light and ionizing radiation are the two main forms of radiation carcinogens which can induce cancer. Also, radiation carcinogens may act to enhance the effect of another carcinogen (co-carcinogens) and may have sequential stages of initiation, promotion and progression in their evolution. They cause damages to the DNA of the cell.
- 2. Non-radiation physical carcinogenesis:** Mechanical injury to the tissues such as from stones in the gallbladder, has been suggested as the cause of increased risk of carcinoma.

D. Biologic Carcinogenesis

Viruses and human cancer: Presently, about 20% of all human cancers worldwide are virally induced.

Benign tumors

- i. Human wart (papilloma) caused by human papillomavirus.
- ii. Molluscum contagiosum caused by poxvirus.

Malignant tumors

- i. Burkitt's lymphoma by Epstein-Barr virus.
- ii. Nasopharyngeal carcinoma by Epstein-Barr virus.
- iii. Primary hepatocellular carcinoma by hepatitis B virus and hepatitis C virus.
- iv. Cervical cancer by high risk human papilloma-virus types (HPV 16 and 18).
- v. Kaposi's sarcoma by human herpesvirus type 8 (HHV-8).
- vi. Pleural effusion B cell lymphoma by HHV-8.
- vii. Adult T cell leukemia and lymphoma by HTLV-I.
- viii. T cell variant of hairy cell leukemia by HTLV-II.

Q. 2. Write a short note on proto-oncogenes.

(TNMGR, March 2010)

Ans. Proto-oncogenes are growth-promoting genes, i.e. they encode for cell proliferation pathway. In cancer, the transformed cells are produced by abnormal cell growth due to genetic damage to these normal controlling genes. Mutated form of normal proto-oncogene in cancer is called oncogenes. Proto-oncogene becomes activated oncogenes by following mechanisms as under:

- i. By mutation in the proto-oncogene which alters its structure and function.
- ii. By retroviral insertion in the host cell.
- iii. By damage to the DNA sequence that normally regulates growth-promoting signals of proto-oncogene resulting in its abnormal activation.
- iv. Over activity of oncogenes enhances cell proliferation and promotes development of human cancer.

Transformation of proto-oncogene (i.e. normal cell proliferation gene) to oncogenes (i.e. cancer cell proliferation gene) may occur by three mechanisms:

- i. Point mutations, i.e. an alteration of a single base in the DNA chain.
- ii. Chromosomal translocations, i.e. transfer of a portion of one chromosome carrying proto-oncogene to another chromosome and making it independent of growth controls. This is implicated in the pathogenesis of leukemias and lymphomas, e.g. Philadelphia chromosome seen in 95% cases of chronic myelogenous leukemia in which c-ABL

proto-oncogene on chromosome 9 is translocated to chromosome 22.

Oncogenes, proto-oncogenes (in bracket) with associated human tumors

a. Growth factors

- i. PDGF- β (SIS): Gliomas, sarcoma.
- ii. TGF- α (RAS): Carcinomas, sarcomas.
- iii. FGF (HST-1): Bowel cancer; INT-2: breast cancer.
- iv. HGF (HGF): Follicular carcinoma of thyroid.

b. Receptors for growth factors

- i. EGF receptors (ERB B1): Squamous cell carcinoma of lung; (ERB B2): Carcinoma of breast, ovary.
- ii. c-KIT receptor (c-KIT): Gastrointestinal stromal tumor.
- iii. RET receptor (RET): MEN type 2A, 2B, medullary carcinoma of thyroid.

c. Cytoplasmic signal transduction proteins

- i. GTP-bound (RAS): Carcinoma of lungs, colon, pancreas.
- ii. Non-receptor tyrosine kinase (BCR-ABL): CML, acute leukemias.

d. Nuclear transcription factors

- i. C-MYC (MYC): Burkitt's lymphoma.
- ii. N-MYC (MYC): Neuroblastoma, small cell carcinoma of lung.
- iii. L-MYC (MYC): Small cell carcinoma of lung.

e. Cell cycle regulatory proteins

- i. Cyclins (Cyclin D): Carcinoma breast, liver, mantle cell lymphoma; (Cyclin E): Carcinoma breast.
- ii. CDKs (CDK4): Glioblastoma, sarcomas.

Q. 3. Write a note on cancer suppressor genes.

(TNMGR, March 2007, 12008)

Ans. The mutation of normal growth suppressor anti-oncogenes results in removal of the brakes for growth; thus the inhibitory effect to cell growth is removed and the abnormal growth continues unchecked. The mechanisms of loss of tumor suppressor actions of genes are due to chromosomal deletions, point mutations and loss of portions of chromosomes.

Major anti-oncogenes implicated in human cancers are

1. RB: Retinoblastoma, osteosarcoma.
2. P53 (TP53): Most human cancers, carcinoma lung, head and neck, colon, breast.
3. TGF- β and its receptor: Carcinoma pancreas, colon, stomach.
4. APC and β -catenin proteins: Carcinoma colon.

5. Others

- i. BRCA 1 and 2: Carcinoma breast, ovary.
- ii. VHL: Renal cell carcinoma.
- iii. WT 1 and 2: Wilm's tumor.
- iv. NF 1 and 2: Neurofibromatosis type 1 and 2.

Q. 4. Write a short note on tumor markers.

(MUHS, May 2015)

Ans. Tumor markers are biochemical assays of products elaborated by the tumor cells in blood or other body fluids. They can be used as an adjunct to the pathologic diagnosis arrived at by other methods and not for primary diagnosis of cancer. Secondly, it can be used for prognostic and therapeutic purposes. Tumor markers include cell surface antigens (or oncofetal antigens), cytoplasmic proteins, enzymes, hormones and cancer antigens.

1. Oncofetal antigens

- i. *Alpha-foetoprotein (AFP)*: Hepatocellular carcinoma.
- ii. *Carcinoembryonic antigen (CEA)*: Cancer of bowel, pancreas, breast.

2. Enzymes

- i. *Prostate acid phosphatase*: Prostatic carcinoma.
- ii. *Neuron specific enolase*: Neuroblastoma.
- iii. *Lactic dehydrogenase (LDH)*: Lymphoma, Ewing's sarcoma.

3. Hormones

- i. *Human chorionic gonadotropin*: Trophoblastic tumors.
- ii. *Calcitonin*: Medullary carcinoma thyroid.
- iii. *Catecholamines and vanillylmandelic acid*: Neuroblastoma, pheochromocytoma.
- iv. *Ectopic hormone production*: Paraneoplastic syndromes.

4. Cancer associated proteins

- i. CA-125: Ovary
- ii. CA 15-3: Breast
- iii. CA 19-9: Colon, pancreas, breast
- iv. CD30: Hodgkin's disease
- v. CD25: Hairy cell leukemia, adult T cell leukemia lymphoma.
- vi. *Monoclonal immunoglobulins*: Multiple myeloma, other gammopathies.
- vii. *Prostate specific antigen*: Prostate carcinoma.

Q. 5. Write a short note on grading and staging of tumors. (TNMGR, March 2011; PAHER, April 2013)

Ans. Grading is defined as the gross and microscopic degree of differentiation of the tumor, while staging means extent of spread of the tumor within the patient. Thus, grading is histologic while staging is clinical.

Grading: Cancers may be graded grossly and microscopically. Gross features like exophytic or fungating appearance are indicative of less malignant growth than diffusely infiltrating tumors. However, grading is largely based on 2 important histologic features: The degree of anaplasia, and the rate of growth. Based on these features, cancers are categorized from grade I as the most differentiated, to grade III or IV as the most undifferentiated or anaplastic. Broders' grading is as under:

Grade I: Well-differentiated (less than 25% anaplastic cells).

Grade II: Moderately-differentiated (25–50% anaplastic cells).

Grade III: Moderately-differentiated (50–75% anaplastic cells).

Grade IV: Poorly-differentiated or anaplastic (more than 75% anaplastic cells).

However, grading of tumors has several shortcomings.

1. It is subjective.
2. The degree of differentiation may vary from one area of tumor to the other.

Staging: The extent of spread of cancers can be assessed by 3 ways—by clinical examination, by investigations, and by pathologic examination of the tissue removed. Two important staging systems currently followed are: TNM staging and AJC staging.

TNM staging (T for primary tumor, N for regional nodal involvement, and M for distant metastases) was developed by the UICC (Union Internationale Centre Cancer, Geneva). For each of the 3 components, namely T, N and M, numbers are added to indicate the extent of involvement, as under.

T: Primary tumor

Tx: Primary tumor cannot be assessed.

T0: No evidence of primary tumor.

Tis: Carcinoma in situ.

T1: Tumor 2 cm or less in greatest dimension.

T2: Tumor more than 2 cm but not more than 4 cm in greatest dimension.

T3: Tumor more than 4 cm in greatest dimension.

T4a (lip): Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (chin or nose), muscle of tongue, maxillary sinus, skin of face (oral cavity).

T4b: Tumor invades masticator space, pterygoid plates or skull base or internal carotid artery.

N: Regional lymph nodes

Nx: Regional lymph nodes cannot be assessed.

N0: No regional lymph nodes.

N1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension.

N2:

N2a: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension.

N2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.

N2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.

N3: Metastasis in a lymph node more than 6 cm in greatest dimension.

M: Distant metastasis

Mx: Distant metastasis cannot be assessed.

M0: No distant metastasis.

M1: Distant metastasis.

Stage grouping

Stage 0: Tis N0 M0

Stage I: T1 N0 M0

Stage II: T2 N0 M0

Stage III: T1, T2 N1 M0; T3 N0, N1 M0

Stage IVA: T1, T2, T3 N2 M0; T4a N0, N1, N2 M0

Stage IVB: Any T N3 M0; T4b any N M0

Stage IVC: Any T any N M1

AJC staging: American Joint Committee staging divides all cancers into stage 0 to IV, and takes into account all the 3 components of the preceding system (primary tumor, nodal involvement and distant metastases) in each stage. TNM and AJC staging systems can be applied for staging most malignant tumors.

Q. 6. Write about immune surveillance against cancer.

(TNMGR, Oct. 1996)

Ans. Cancer immune surveillance is considered to be an important host protection process to inhibit carcinogenesis and to maintain cellular homeostasis. In the interaction of host and tumor cells, three essential phases have been proposed: Elimination, equilibrium and escape, which are designated the 'three Es'. Several immune effector cells and secreted cytokines play a critical role in pursuing each process. Nascent transformed cells can initially be eliminated by an innate immune response such as by natural killer cells. During tumor progression, even though an adaptive immune response can be provoked by antigen-specific T cells, immune selection produces tumor cell variants that lose major histocompatibility complex class I and II antigens and decreases amounts of tumor antigens in the

equilibrium phase. Furthermore, tumor-derived soluble factors facilitate the escape from immune attack, allowing progression and metastasis.

Mechanisms of immune surveillance

TCR: T cell receptor; IFN: Interferon; Stat 1: Signal transducers and activators of transcription 1; NKT: Natural killer T cell; IFNGR: Interferon gamma receptor; CTL: Cytotoxic T lymphocyte; NK: Natural killer; MCA: Methylcholanthrene; TPA: 12-O-tetradecanoylphorbol-13-acetate; DMBA: 7,12-dimethylbenzanthracene (see table on next page).

6. DISEASES OF ORAL CAVITY**Q. 1. Write a short note on candidiasis.**

(TNMGR, March 2007)

Ans. Candidiasis is an opportunistic fungal infection caused most commonly by *Candida albicans* and occasionally by *Candida tropicalis*. In human beings, *Candida* species are present as normal flora of the skin and mucocutaneous areas, intestines and vagina. The organism becomes pathogenic when the balance between the host and the organism is disturbed.

Predisposing factors: Impaired immunity, prolonged use of oral contraceptives, long-term antibiotic therapy, corticosteroid therapy, diabetes mellitus, obesity, pregnancy, etc.

Morphologic Features

1. **Oral thrush:** This is the commonest form of mucocutaneous candidiasis seen especially in early life. Full fledged lesions consist of creamy white pseudomembrane composed of fungi covering the tongue, soft palate, and buccal mucosa. In severe cases, ulceration may be seen.
2. **Candidal vaginitis:** Vaginal candidiasis or monilial vaginitis is characterized by thick, yellow, curdy discharge. The lesions form pseudomembrane of fungi on the vaginal mucosa. They are quite pruritic and may extend to involve the vulva and the perineum.
3. **Cutaneous candidiasis:** Candidal involvement of nail folds producing change in the shape of nail plate (paronychia) and colonization in the intertriginous areas of the skin, axilla, groin, infra- and intermammary, intergluteal folds and interdigital spaces are some of the common forms of cutaneous lesions caused by *Candida albicans*.
4. **Systemic candidiasis:** Invasive candidiasis is rare and is usually a terminal event of an underlying disorder associated with impaired immune system. The

Target gene	Target/effector cell	Tumor formation
TCR J alpha 281	NKT	MCA-induced sarcoma
TCR delta	Gamma delta T	MCA-induced sarcoma DMBA-induced skin tumor
TCR beta	Alpha beta T	MCA-induced sarcoma
TCR beta/TCR delta	T/gamma delta T	Reduced latency
IFN-gamma	IFN-gamma	MCA-induced sarcoma Spontaneous lymphoma Lung adenocarcinoma
Stat 1	IFK-gamma R-signalling	MCA-induced sarcoma
Perforin	CTL/NK	MCA-induced sarcoma Spontaneous lymphoma TPA/DMBA-induced sarcoma
RAG-2/Stat 1	T/B/NKT/IFN-signalling	MCA-induced sarcoma
IFNGR1 or Stat 1/p53	IFN-gamma R-signalling/tumor susceptibility	More rapid tumor formation/wider tumor spectrum
Perforin/p53 lymphoma	CTL/NK/tumor susceptibility	Enhances susceptibility to lymphoma

organisms gain entry into the body through an ulcerative lesion on the skin and mucosa or may be introduced by iatrogenic means such as via intravenous infusion, peritoneal dialysis or urinary catheterization. The lesions of systemic candidiasis are most commonly encountered in kidneys as ascending pyelonephritis and in heart as candidal endocarditis.

Q. 2. Write a short note on actinomycosis.

(TNMGR, Nov. 2001)

Ans. Actinomycosis is a chronic suppurative disease caused by anaerobic bacteria, *Actinomyces israelii*. The organisms are commensals in the oral cavity, alimentary tract and vagina. The infection is always endogenous in origin and not by person-to-person contact.

Morphologic Features

Four types

1. *Cervicofacial actinomycosis*: This is the commonest form (60%) and has the best prognosis. The infection enters from tonsils, carious teeth, periodontal disease or trauma following tooth extraction. Initially, a firm swelling develops in the lower jaw ('lumpy jaw'). In time, the mass breaks down and abscesses and multiple sinuses are formed. The discharging pus contains typical tiny yellow *sulfur granules*. The infection may extend into adjoining soft tissues as well as may destroy the bone.
2. *Thoracic actinomycosis*: Due to aspiration of the organism from oral cavity or extension of infection

from abdominal or hepatic lesions. Initially, the disease resembles pneumonia but subsequently the infection spreads to the whole of lung, pleura, ribs and vertebrae.

3. *Abdominal actinomycosis*: This type is common in appendix, cecum and liver. The abdominal infection results from swallowing of organisms from oral cavity or extension from thoracic cavity.
4. *Pelvic actinomycosis*: Infection in the pelvis occurs as a complication of intrauterine contraceptive devices (IUCDs).

Microscopically

- i. The inflammatory reaction is a granuloma with central suppuration. There is formation of abscesses in the centre of lesions and at the periphery chronic inflammatory cells, giant cells and fibroblasts are seen.
- ii. The centre of each abscess contains the bacterial colony, 'sulfur granule', characterized by radiating filaments (hence previously known as **ray fungus**) with hyaline, eosinophilic, club-like ends representative of secreted immunoglobulins.
- iii. Bacterial stains reveal the organisms as gram-positive filaments, nonacid-fast, which stain positively with Gomori's methenamine silver (GMS) staining.

Treatment

Intramuscular injection of penicillin or tetracycline 500 mg every 6 hours.

Q. 3. Classify ulcerative lesions of the oral cavity and describe the clinical features.

(Bombay Uni., Oct. 1985; TNMGR, April 2013)

Ans.

a. Acute multiple ulceration

1. *Herpes virus infections*: Primary herpes simplex virus infections, coxsackievirus infections, varicella-zoster virus infection
2. Erythema multiforme
3. Contact allergic stomatitis
4. Oral ulcers secondary to cancer chemotherapy
5. Acute necrotizing ulcerative gingivitis (ANUG)

b. Recurring oral ulcers

1. Recurrent aphthous stomatitis
2. Behçet's syndrome
3. Magic syndrome
4. Recurrent herpes simplex virus infection

c. Chronic multiple ulcers

1. Pemphigus.
2. Subepithelial bullous dermatoses.
3. Herpes simplex virus infection in immunosuppressed patients

d. Solitary ulcers

1. Traumatic ulcer
2. Eosinophilic granuloma
3. Histoplasmosis
4. Blastomycosis
5. Mucormycosis

Q. 4. Classify parotid tumors. (TNMGR, April 1995)

Ans.

Classification

a. Adenomas

1. Pleomorphic adenoma
2. Myoepithelial adenoma
3. Basal cell adenoma
4. Warthin tumor
5. Oncocytoma
6. Ductal papilloma
7. Cystadenoma
8. Sebaceous adenoma

b. Carcinomas

1. Acinic cell carcinoma.
2. Mucoepidermoid carcinoma.
3. Adenoid cystic carcinoma.
4. Polymorphous low grade adenocarcinoma.
5. Oncocytic carcinoma.

6. Salivary duct carcinoma.
7. Adenocarcinoma.
8. Myoepithelial carcinoma.
9. Carcinoma in pleomorphic adenoma.
10. Squamous cell carcinoma.

c. Nonepithelial tumors

d. Malignant lymphomas

e. Secondary tumors

f. Unclassified tumors

g. Tumor-like lesions

1. Sialadenosis
2. Oncocytosis
3. Benign lymphoepithelial lesion
4. Salivary gland cysts
5. Kuttner's tumor
6. Cystic lymphoid hyperplasia in AIDS.

Q. 5. Write about maxillary sinus diseases.

(TNMGR, April 2012)

Ans.

a. Congenital abnormalities

1. *Development variations*: Aplasia, hypoplasia.
2. *Facial clefts and syndromes*: Cleft lip/cleft face syndrome, crouzen syndrome, etc.
3. Choanal atresia.
4. *Osteomeatal variations*: Anomalies of turbinate, uncinate process, etc.

b. Inflammatory diseases and infection

1. Acute sinusitis
2. Chronic sinusitis
3. Sinonasal polyps
4. Antrochoanal polyp
5. Mucus retention cyst
6. Fungal sinusitis
7. Granulomatous diseases

c. Trauma

1. Isolated fractures
2. Complex facial fractures
3. Transfacial fractures

d. Benign neoplasm

1. Papilloma
2. Juvenile angiofibroma

e. Malignant neoplasm

1. Squamous cell carcinoma
2. Adenocarcinoma
3. Lymphoma
4. Malignant melanoma
5. Osteogenic sarcoma
6. Chondrosarcoma

7. Rhabdosarcoma
8. Olfactory neuroblastoma

f. Fibro-osseous lesions

1. Osteoma
2. Fibrous dysplasia
3. Ossifying fibroma
4. Cherubism

g. Odontogenic cysts and tumors

1. *Odontogenic cysts*: Primordial, dentigerous, radicular, odontogenic keratocyst, calcifying odontogenic cyst.
2. *Odontogenic tumors*: Ameloblastoma, odontoma, cementoma.

h. Miscellaneous lesions

1. Thalassemia
2. Giant cell reparative granuloma
3. Hemangiopericytoma.

Q. 6. Write short note on differential diagnosis of neck swellings.
(HP, May 2012)

Ans.

1. Cervical lymph nodes
2. Benign lymphoid hyperplasia
3. Acute lymphadenitis
4. Fibrosed lymph nodes
5. Sebaceous cysts
6. Space abscess
7. Salivary gland inflammations
8. Lipomas
9. Salivary gland tumors
10. Thyroid gland enlargements
11. Benign systemic lymph node enlargements—
infectious mononucleosis, viral diseases
12. Epidermoid and dermoid cysts
13. Metastatic tumors
14. Thyroglossal cyst
15. Cystic hygromas
16. Lymphomas
17. Branchial cysts.

Q. 7. Write a short note on xerostomia.

(RGUHS, Oct. 2010, Nov. 2011)

Ans. Xerostomia or dryness of mouth is not a disease itself; rather it can be symptom of certain diseases.

Etiology

a. Temporary causes

1. *Psychological*: anxiety and depression.
2. Sialolith.
3. *Sialadenitis*: Mumps, postoperative parotitis, chronic sialadenitis.
4. *Drugs*: Anticholinergic, sympathomimetic, etc.

b. Permanent causes

1. *Salivary gland disorders*: Aplasia, Sjögren syndrome.
2. *Systemic disorders*: Diabetes, Parkinson's disease, cystic fibrosis, etc.
3. Radiotherapy.
4. Surgical desalivation.

Clinical Features

1. Pain and swelling of the glands
2. Dryness of mouth
3. Difficulty in speech, swallowing
4. More chances of caries development
5. Dry, atrophic, pale oral mucosa
6. Soreness and burning

Treatment

Eliminate the underlying cause. Use of sialogogue, sugar free chewing gums.

Q. 8. Write a short note on cancrum oris.

(TNMGR, April 1995)

Ans. Cancrum oris/noma/gangrenous stomatitis is a rapidly spreading mutilating, gangrenous stomatitis that occurs usually in debilitated or nutritionally deficient persons.

Predisposing factors

1. Malnutrition
2. Debilitating infections
3. Blood dyscrasias

Causative organism: Vincent's organism.

Clinical Features

1. Usually begins as small ulcer of mucosa.
2. The ulcer rapidly spreads and involves the surrounding tissue of jaw, lips, and cheeks by gangrenous necrosis.
3. The initial site is around fixed bridge or crown.
4. The overlying skin becomes inflamed, edematous and finally necrotic.
5. The line of demarcation develops between healthy and dead tissue.
6. The large masses of tissue slough out, leaving the jaw exposed.
7. Extremely foul odor from gangrenous tissue.
8. High grade fever.
9. Death may occur from toxemia or pneumonia.

Treatment

Treatment of predisposing factors along with high doses of antibiotics.

Q. 9. Write a short note on salivary calculi.

(TNMGR, April 1995)

Ans. Salivary calculi is the occurrence of calcareous concretions in the salivary ducts or glands.

Clinical Features

1. May occur at any age.
2. Most commonly associate with submandibular gland.
3. Severe pain and swelling before, during and after meals.
4. Sometime totally asymptomatic, if it small.
5. Sialolith may be round, ovoid, or elongated.

Composition

Calcium phosphate, calcium carbonate, soluble salts, organic matter, water.

Treatment

Small stones can be removed by manipulation. Large stones require surgical removal.

Q. 10. Write a short note on submucous fibrosis.

(BFUHS, Nov. 2009; TNMGR, April 2013)

Ans. Oral submucous fibrosis is defined as chronic, insidious disease affecting any part of the oral cavity and sometimes the pharynx, occasionally preceded by and/or associated with vesicle formation, it is always associated with the juxtaepithelial inflammatory reaction followed by a fibroelastic change of lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat.

Etiology

Areca nut chewing.

Clinical Features

1. Burning sensation on eating spicy food.
2. Appearance of blisters on palate.
3. Excessive salivation with altered taste sensation.
4. Blanched oral mucosa.
5. Appearance of fibrotic bands which are palpable.
6. Progressive reduced mouth opening.

Grading**Grading of trismus**

1. *Severe*: <20 mm.
2. *Moderate*: 20–40 mm
3. *Mild*: >40 mm.

Grading of oral submucous fibrosis

1. *Grade I*: Only blanching of oral mucosa.

2. *Grade II*: Burning sensation, dryness of mouth, vesicles and ulcers.
3. *Grade III*: Grade II plus restricted mouth opening.
4. *Grade IV*: Grade III plus palpable fibrotic bands all over the mouth without involvement of the tongue.
5. *Grade V*: Grade IV plus involvement of tongue.
6. *Grade VI*: Oral submucous fibrosis with histologically proven oral cancer.

Investigations

Increase ESR, low hemoglobin, eosinophilia, decreased serum iron, increase in total iron binding capacity.

Management

1. *Nutritional support*: High protein diet with multi-vitamins.
2. *Immunomodulatory drugs*: Glucocorticoids, placental extracts.
3. *Physiotherapy*: Forceful mouth opening, heat therapy.
4. *Local drug delivery*: Injections of corticosteroids, placental extract, hyaluronidase, collagenase.
5. Combined therapy.
6. Surgical management.

Q. 11. Write a short note on denture stomatitis.

(BFUHS, Nov. 2008)

Ans. Denture stomatitis is areas of redness confined to denture bearing mucosa.

Etiology

1. History of wearing dentures during sleep.
2. Chronic trauma because of ill fitting denture.
3. Inadequate denture curing.
4. Poor oral hygiene.

Clinical Features

1. The denture bearing mucosa becomes smooth and red.
2. Usually asymptomatic.
3. *Type I*: Localized redness confined to denture bearing palatal mucosa.
4. *Type II*: Diffuse redness of the mucosa.
5. *Type III*: Redness with nodular, papillary growth.

Management

1. Correction of irregularities of denture
2. Rebasing of denture
3. Construction of dentures
4. Antifungal therapy
5. Oral hygiene maintenance.

Q. 12. Write a short note on Ludwig's angina.

(TNMGR, Oct. 2013)

Ans. Ludwig's angina is firm, brawny cellulitis involving submandibular, sublingual and submental spaces, bilaterally.

Etiology

1. Odontogenic infection
2. *Iatrogenic*: Use of contaminated needle during local anesthesia
3. Trauma
4. Osteomyelitis

Clinical Features

1. Patient is febrile, dehydrated
2. Marked dysphagia, impaired speech
3. Hard brawny swelling of submandibular region
4. Severe trismus
5. Airway obstruction
6. Raised floor of mouth

Management

It is a life-threatening emergency situation. Management includes early diagnosis, maintenance of patent airways, intense and prolonged antibiotic therapy, extraction of offending tooth, and surgical drainage or decompression of facial spaces.

Q. 13. Write a short note on Bell's palsy.

(KUHS, June 2013)

Ans. It is as an abrupt, isolated, unilateral, idiopathic paralysis of facial nerve.

Etiology

1. Idiopathic mostly
2. Infections—HSV

Clinical Features

1. Usually unilateral
2. Female affected more than males
3. Drooping of corner of mouth
4. Watering of eyes
5. Inability to close the eye
6. Loss of forehead wrinkling
7. Inability to raise the eyebrow
8. Typical mask-like expressionless face
9. Difficulty in eating and speech with altered taste.

Treatment

Most of the cases are mild, and regresses within months. Use of vasodilator drugs. Administration of nicotinic acid.

Q. 14. Write in detail about HIV/AIDS.

(TNMGR, March 2010)

Ans. The disease has now attained pandemic proportions involving all continents. Half of all serologically positive cases are in women while children comprise 5% of all cases.

Etiologic Agent

AIDS is caused by an RNA retrovirus called human immunodeficiency virus (HIV) which is a type of human T cell leukemia-lymphoma virus (HTLV). HIV has tropism for CD4 molecules present on sub-population of T cells which are the particular targets of attack by HIV. HIV is cytolytic for T cells causing immunodeficiency (cytopathic virus). Two forms of HIV have been described, HIV1 being the etiologic agent for AIDS in the US and Central Africa, while HIV2 causes a similar disease in West Africa and parts of India.

Routes of Transmission

Transmission of HIV infection occurs by:

1. Sexual transmission.
2. *Transmission via blood and blood products*:
 - i. Intravenous drug abusers
 - ii. Hemophiliacs
 - iii. Recipients of HIV-infected blood and blood products.
3. Perinatal transmission
4. Occupational transmission
5. *Transmission by other body fluids*: Saliva, tears, sweat and urine, semen, vaginal secretions, cervical secretions, breast milk, CSF, synovial, pleural, peritoneal and pericardial fluid.

Pathogenesis

The pathogenesis of HIV infection is largely related to the depletion of CD4+ T cells (helper T cells) resulting in profound immunosuppression.

1. **Selective tropism for CD4 molecule receptor**: gp120 envelope glycoprotein of HIV has selective tropism for cells containing CD4 molecule receptor on their surface; these cells most importantly are CD4+ T cells (T helper cells); other such cells include monocyte-macrophages, microglial cells, epithelial cells of the cervix, Langerhans, cells of the skin and follicular dendritic cells.
2. **Internalization**: gp120 of the virion combines with CD4 receptor, but for fusion of virion with the host cell membrane, a chemokine coreceptor (CCR) is necessary. Once HIV has combined with CD4 receptor and CCR, gp41 glycoprotein of envelope is internalized in the CD4+ T cell membrane.

3. **Uncoating and viral DNA formation:** Once the virion has entered the T cell cytoplasm, reverse transcriptase of the viral RNA forms a single-stranded DNA. Using the single-stranded DNA as a template, DNA polymerase copies it to make it double-stranded DNA, while destroying the original RNA strands.
4. **Viral integration:** Viral integrase protein inserts the viral DNA into nucleus of the host T cell and integrates in the host cell DNA. At this stage, viral particle is termed as HIV provirus.
5. **Viral replication:** HIV provirus having become part of host cell DNA, host cell DNA transcripts for viral RNA with presence of tat gene. Multiplication of viral particles is further facilitated by release of cytokines from T helper cells (CD4+ T cells): TH 1 cells elaborating IL-2 and IFN- γ , and TH2 cells elaborating IL-4, IL-5, IL-6, IL-10.
6. **Latent period and immune attack:** In an inactive infected T cell, the infection may remain in latent phase for a long time, accounting for the long incubation period.
7. **CD4+ T cell destruction:** Viral particles replicated in the CD4+ T cells start forming buds from the cell wall of the host cell. As these particles detach from the infected host cell, they damage part of the cell membrane of the host cell and cause death of host CD4+ T cells by apoptosis.
8. **Viral dissemination:** Release of viral particles from infected host cell spreads the infection to more CD4+ host cells and produces viremia. Through circulation, virus gains entry to the lymphoid tissues (lymph nodes, spleen) where it multiplies further, and is the dominant site of virus reservoir rather than circulation.
9. **Impact of HIV infection on other immune cells:** HIV infects other cells of the host immune system and also affects non-infected lymphoid cells.

Natural History

Generally the biologic course passes through following 3 phases:

1. **Acute HIV syndrome (3–12 weeks)**
 - i. High levels of plasma viremia due to replication of the virus.
 - ii. Virus-specific immune response by formation of anti-HIV antibodies (seroconversion) after 3 weeks of initial exposure to HIV.
 - iii. Initially, sudden marked reduction in CD4+ T cells (helper T cells) followed by return to normal levels.
 - iv. Rise in CD8+ T cells (cytotoxic T cells).

- v. Appearance of self-limited non-specific acute viral illness in 50–70% of adults within 3–6 weeks of initial infection. Manifestations include sore throat, fever, myalgia, skin rash, and sometimes, aseptic meningitis. These symptoms resolve spontaneously in 2–3 weeks.

2. Middle chronic phase (10–12 years)

- i. With passage of time viral load increases
- ii. Chronic stage, may continue as long as 10 years.
- iii. CD 4+ T cells continue to proliferate but net result is moderate fall in CD4+ T cell counts.
- iv. Cytotoxic CD8+ T cell count remains high.
- v. Clinically, it may be a stage of latency and the patient may be asymptomatic, or may develop mild constitutional symptoms and persistent generalized lymphadenopathy.

3. Final crisis phase: Full-blown AIDS

- i. Marked increase in viremia.
- ii. The time period from HIV infection through chronic phase into full-blown AIDS may last 7–10 years and culminate in death.
- iii. CD4+ T cells are markedly reduced (below 200 per μ l). The average survival after the onset of full-blown AIDS is about 2 years.

Revised CDC HIV Classification System

The Centers for Disease Control and Prevention (CDC), US in 1993 revised the classification system for HIV infection based on 2 parameters: Clinical manifestations and CD4+ T cell counts. According to this classification, HIV-AIDS has 3 categories: A, B and C.

Category A: Includes a variety of conditions: Asymptomatic case, persistent generalized lymphadenopathy (PGL), and acute HIV syndrome. CD4+ T cell counts in clinical category A are $>500/\mu$ l.

Category B: Includes symptomatic cases and includes conditions secondary to impaired cell-mediated immunity, e.g. bacillary dysentery, mucosal candidiasis, fever, oral hairy leukoplakia, ITP, pelvic inflammatory disease, peripheral neuropathy, cervical dysplasia and carcinoma *in situ* cervix, etc. CD4+ T cell counts in clinical category B are $200\text{--}499/\mu$ l.

Category C: This category includes conditions listed for AIDS surveillance case definition. These are mucosal candidiasis, cancer uterine cervix, bacterial infections (e.g. tuberculosis), fungal infections (e.g. histoplasmosis), parasitic infections (e.g. *Pneumocystis carinii* pneumonia), malnutrition and wasting of muscles, etc. CD4+ T cell counts in clinical category C are $<200/\mu$ l and are indicator for AIDS.

Clinical Manifestations

1. **Wasting syndrome:** Wasting syndrome defined as 'involuntary loss of body weight by more than 10%'. It occurs due to malnutrition, increased metabolic rate, malabsorption, anorexia, and ill-effects of multiple opportunistic infections.
2. **Persistent generalized lymphadenopathy:** PGL is defined as presence of enlarged lymph nodes >1 cm at two or more extra inguinal sites for >3 months without an obvious cause.
3. **Gastrointestinal lesions and manifestations:** Chronic watery or bloody diarrhea, oral, oropharyngeal and esophageal candidiasis, anorexia, nausea, vomiting, mucosal ulcers, abdominal pain. Advance cases may develop secondary tumors occurring in GIT (e.g. Kaposi's sarcoma, lymphoma).
4. **Pulmonary lesions and manifestations:** Features are largely due to opportunistic infections causing pneumonia, e.g. with *Pneumocystis carinii*, *M. tuberculosis*, CMV, histoplasma, and staphylococci. Lung abscess too may develop. Other pulmonary manifestations include adult respiratory distress syndrome and secondary tumors (e.g. Kaposi's sarcoma, lymphoma).
5. **Mucocutaneous lesions and manifestations:** Mucocutaneous viral exanthem in the form of erythematous rash is seen at the onset of primary infection itself. Other mucocutaneous manifestations are allergic (e.g. drug reaction, seborrheic dermatitis), infectious (viral infections such as herpes, varicella-zoster, EB virus, HPV; bacterial infections such as *M. avium*, *Staph. aureus*; fungal infections such as *Candida*, *Cryptococcus*, *Histoplasma*) and neoplastic (e.g. Kaposi's sarcoma, squamous cell carcinoma, basal cell carcinoma, cutaneous lymphoma).
6. **Hematologic lesions and manifestations:** Anemia, leukopenia, and thrombocytopenia.
7. **CNS lesions and manifestations:** HIV encephalopathy or AIDS associated dementia complex, meningitis, demyelinating lesions of the spinal cord, and peripheral neuropathy and lymphoma of the brain.
8. **Gynecologic lesions and manifestations:** Monilial (candidal) vaginitis, cervical dysplasia, carcinoma cervix, and pelvic inflammatory disease.
9. **Renal lesions and manifestations:** Nephropathy and genitourinary tract infections including pyelonephritis.
10. **Hepatobiliary lesions and manifestations:** Drug-induced hepatic injury, steatosis, granulomatous hepatitis and opportunistic infections.
11. **Cardiovascular lesions and manifestations:** HIV-associated cardiomyopathy, pericardial effusion, lymphoma and Kaposi's sarcoma.
12. **Ophthalmic lesions:** Opportunistic infections (e.g. CMV retinitis), HIV retinopathy, and secondary tumors.
13. **Musculoskeletal lesions:** Osteoporosis, osteopenia, septic arthritis, osteomyelitis and polymyositis.
14. **Endocrine lesions:** Due to dyslipidemia, hyperinsulinemia and hyperglycemia.

Diagnosis of HIV/AIDS

1. Tests for establishing HIV infection

i. Antibody tests

- a. ELISA—initial screening is done by serologic test for antibodies by enzyme-linked immunosorbent assay (ELISA) against gag and env proteins.
- b. Western blot—if ELISA is positive, confirmation is done by Western blot for presence of specific antibodies against all three HIV antigens: gag, pol and env.

ii. Direct detection of HIV

- a. p24 antigen capture assay.
- b. HIV RNA assay methods by reverse transcriptase (RT) PCR branched DNA, nucleic acid sequence-based amplification (NucliSens).
- c. DNA-PCR by amplification of proviral DNA.
- d. Culture of HIV from blood monocytes and CD4+ T cells.

2. Tests for defects in immunity: These tests are used for diagnosis as well as for monitoring treatment of cases.

- i. CD4+ T cell counts—progressive fall
- ii. Rise in CD8+ T cells
- iii. Reversal of CD4+ to CD8+ T cell ratio
- iv. Lymphopenia
- v. Polyclonal hypergammaglobulinemia
- vi. Increased β_2 microglobulin levels
- vii. Platelet count revealing thrombocytopenia.

3. Tests for detection of opportunistic infections and secondary tumors: By aspiration or biopsy methods.

Q. 15. Write a short note on addiction and dental diseases. (TNMGR, April 2013)

Ans.

1. Oral health problems associated with opiates

- a. Tooth loss
- b. Tooth extractions
- c. Generalized tooth decay especially on smooth and cervical surfaces

- d. Salivary hypofunction
- e. Xerostomia
- f. Burning mouth
- g. Taste impairment
- h. Eating difficulties
- i. Mucosal infections
- j. Periodontal diseases

Heroin users show poor oral health in terms of caries and periodontal diseases. Caries in these patients is darker and usually limited to buccal and labial surfaces. Other oral conditions related to opioid addiction include bruxism, candidiasis, and mucosal dysplasia.

2. **Oral health problems associated with cannabis:** Cannabis abuse, mainly hashish and marijuana, leads to increased risk of oral cancer, dry mouth, and periodontitis. Side-effects of cannabis to include xerostomia, leukoedema, high prevalence of *Candida albicans* but not candidiasis, and higher DMF scores.
3. **Oral health problems associated with stimulants:** Stimulants include amphetamine, methamphetamine, cocaine, and crack-cocaine. Cocaine snoring is associated with nasal septum perforation, changes in sense of smell, chronic sinusitis, and perforation of the palate. Oral administration of cocaine may result in gingival lesions. Bruxism is a common complication in cocaine users leading to dental attrition. Crack-cocaine smoking produces burns and sores on the lips, face, and inside of the mouth which may increase the risk of oral transmission of HIV. Methamphetamine abusers show bruxism, excessive tooth wear, xerostomia, and rampant caries (so-called meth mouth).
4. **Oral health problems associated with hallucinogens:** Hallucinogens such as ecstasy and LSD (lysergic acid diethylamide) result in several oral complications including dry mouth, bruxism, and problems associated with malnutrition caused by drug-induced anorexia, chewing, grinding, and temporomandibular joint (TMJ) tenderness are frequently reported by ecstasy users.
5. **Oral health problems associated with club drugs:** Club drugs including methylenedioxymethamphetamine (MDMA), ketamine, gamma-hydroxybutyrate (GHB), and flunitrazepam are chemical substances used mainly by young people in recreational settings such as dance clubs and rave parties. These drugs are associated with dry mouth and bruxism, increased risk of dental erosion, ulcers, vestibular swelling, edema, and necrosis.
6. **Indirect effects of drugs on oral health:** It is difficult to identify and isolate the root causes of oral diseases

among addicts, since they show a variety of unhealthy behaviors. Poor oral hygiene, increased sugar intake, and inappropriate nutrition are examples.

Oral health and HIV transmission: Illicit drugs such as methamphetamines may lead to an increase in risky sexual behaviors resulting in the spread of infectious diseases such as HIV and AIDS.

Barriers against oral health promotion among drug addicts

1. It is difficult to access drug addicts as a target population.
2. In addition to problems with drug abusers' cooperation with and compliance in oral health studies, problems with their long-term follow-up are common.
3. Finally, lack of appropriate policies to improve access to oral health services.
4. Poor collaboration between dental and general health care sectors serving drug addicts.

Dentists should be empowered in the following domains to provide treatment services for addicts

- a. Diagnosis and management of oral problems in addicts.
- b. Management of systemic disorders related to addiction during dental treatments.
- c. Behavioral and psychological management of addicts during dental treatments.
- d. Encouraging dentists' positive attitude toward addicts.
- e. Cross-infection control of blood-borne diseases.

Q. 16. Write a short note on enamel hypoplasia.

(TNMGR, Sept. 2008; RGUHS, Nov. 2011)

Ans. Enamel hypoplasia is defined as an incomplete formation of the organic enamel matrix of teeth.

Types

a. Hereditary

Amelogenesis imperfecta: Hypoplastic, hypocalcified, hypomaturation.

b. Environmental

1. *Nutritional deficiency:* Vitamins A, C and D.
2. *Exanthematous diseases:* Measles, chickenpox, scarlet fever.
3. Congenital syphilis.
4. Hypocalcemia.
5. *Birth injury:* Prematurity, Rh hemolytic disease.
6. Local infection.
7. Local trauma.

8. *Ingestion of chemicals*: Fluorides.

9. Idiopathic causes.

Clinically, in mild cases it appears as small grooves, pits or fissures on the enamel surface. In severe cases, enamel exhibit deep pits across the tooth surface with loss of enamel.

Management

Bleaching, laminate and veneering and capping in severe cases.

Q. 17. Write a short note on odontogenic keratocyst.
(RGUHS, Oct. 2010)

Ans. Odontogenic keratocyst is derived from the remnants of dental lamina, with biological behavior like a neoplasm, with a distinctive lining of 6–10 cells in thickness and that exhibits a basal cell layer of palisaded cells and a surface of corrugated parakeratin.

Clinical Features

1. It may occur in any age (10–90 years).
2. Peak incidence in 2–3 decades.
3. Mandible is affected more than maxilla.
4. In mandible, molar ramus angle area is most commonly involved.
5. In maxilla, molar area is most commonly involved.
6. Pain, soft tissue swelling, neurologic manifestations.
7. Radiographically, unilocular radiolucency with well defined peripheral rim.

Management

Surgical excision.

Q. 18. Describe the fibro-osseous lesion affecting the jaws.
(RGUHS, May 2011)

Ans.

- a. *Cemento-osseous dysplasia*
 1. Periapical cemento-osseous dysplasia
 2. Focal cemento-osseous dysplasia
 3. Familial cemento-osseous dysplasia
- b. *Fibrous dysplasia*
 1. Monostotic
 2. Polyostotic
 3. Craniofacial
- c. Ossifying fibroma.
- d. Cherubism.

Q. 19. Describe the fungal infections affecting the oral cavity.
(RGUHS, May 2011; UHSR, April 2013)

Ans.

1. **Candidiasis**: Caused by *Candida albicans*. It is an opportunistic infection. Predisposing factors include

immunodeficiency, nutritional deficiency, acute and chronic diseases, prolonged antibiotics, radiation therapy, old age, infancy.

i. *Acute*: Pseudomembranous type, atrophic type.

ii. *Chronic*

- a. Chronic hyperplastic candidiasis
- b. Chronic mucocutaneous candidiasis
- c. Chronic atrophic candidiasis

2. **Mucormycosis**: Caused by mucorales.

i. Superficial

ii. *Visceral*

- a. Pulmonary
- b. Gastrointestinal
- c. Rhinocerebral

3. **North American blastomycosis (Gilchrist's disease)**: Caused by *Blastomyces dermatitidis*.

4. **South American blastomycosis (Lutz's disease)**: Caused by *Blastomyces brasiliensis*.

5. **Histoplasmosis (Darling's disease)**: Caused by *Histoplasma capsulatum*.

6. **Cryptococcosis**: Caused by *Cryptococcus neoformans*.

7. **Coccidioidomycosis (valley fever)**: Caused by *Coccidioides immitis*.

8. **Geotrichosis**: Caused by *Geotrichum* species.

Q. 20. Discuss the bite mark analysis.

(RGUHS, May 2011)

Ans. A mark caused by the teeth either alone or in combination with other mouth parts.

Classification

a. *Cameron and Sims classification*:

- i. *Agents*: Human, animal
- ii. *Materials*: Skin, body tissues, foodstuff, other materials

b. *MacDonald's classification*

1. Tooth pressure marks
2. Tongue pressure marks
3. Teeth scrape marks

c. *Webster's classification*

1. *Type I*: Fractured food items with limited depth of penetration.
2. *Type II*: Fractured food items with considerable depth of penetration.
3. *Type III*: Complete penetration with slide marks.

Bite Mark Appearance

Type of injury: Indentations due to compression of skin surface, followed by edema, followed by subcutaneous bleeding (bruise), followed by lacerations.

Identification of the bite marks: A circular or elliptical mark with central ecchymoses—upper and lower incisors/arches. Incisors produce rectangular marks. Canine produces triangular/rectangular marks. Premolar and molar produce spherical or point-shaped bite marks.

Bite Marks Investigations

1. Preliminary relevant questions
2. Evidence collection from the victim
3. Visual examination
4. Photography
5. Saliva swab
6. Impressions
7. Evidence collection from the suspect.

Q. 21. Write a short note on desquamative gingivitis.
(RGUHS, May 2011)

Ans. Desquamative gingivitis is a clinical term used for the condition of the gingiva, characterized by intense redness and desquamation of the surface epithelium.

Etiology

1. **Certain dermatoses:** Cicatricial pemphigoid, pemphigus, lichen planus, epidermolysis bullosa, systemic lupus erythematosus, linear IgA disease.
2. Hormonal influences
3. Abnormal responses to irritation
4. Chronic infections
5. Idiopathic

Clinical Features

1. Occurs in both the genders, in all ages.
2. Predominantly in women of age group 40–55 years.
3. Gingiva is red, swollen and glossy, with loss of stippling.
4. Multiple vesicles with superficial denuded areas, with bleeding on provocation.
5. The normal mucosa is peeled off on rubbing, leaving a raw, bleeding surface.
6. Patient is unable to eat hot, cold and spicy due to sensitive gingiva.
7. Treatment depends on the definitive diagnosis of the disease.

Q. 22. Write a short note on mucocele.
(RGUHS, May 2011)

Ans. Mucocele results from traumatic injury to salivary duct, leading to spillage of mucin into the surrounding tissues. They are not true cyst.

Clinical Features

1. Most commonly found on lower lip, usually lateral to midline.
2. Other sites of involvement are buccal mucosa, anterior ventral tongue, floor of mouth.
3. Commonly seen in all ages.
4. Clinically, it appears as raised, dome-shaped vesicle, with history of rupture, collapse and refilling.
5. Superficial lesions are bluish, translucent; deeper lesions are of normal in color.
6. It arise within a few days, may persists for months.

Treatment

Surgical excision.

Q. 23. Write a short note on brown tumor.
(RGUHS, May 2011)

Ans. Brown tumor/giant cell lesion is due to excessive secretion of parathyroid hormone. This may be due to adenoma, or carcinoma of parathyroid gland.

Clinical Features

1. Three times more common in females
2. Usually affects people of middle age
3. Bone pain, joint stiffness
4. Clinically may resemble giant cell tumor or cystic lesion of the jaw.
5. Pathological fracture may be the first symptom
6. Radiographically, generalized radiolucency, with sharply defined radiolucent areas, ground glass appearance, and loss of lamina dura.
7. Histologically, marked osteoclastic activity, with many areas of yellow-brown hemosiderin (that's why known as Brown tumor) with multinucleated giant cells.
8. Diagnosis is confirmed by hypocalcemia, hypophosphatemia, and elevated levels of alkaline phosphatase.
9. Treatment includes treatment of underlying parathyroid pathology.

Q. 24. Write a short note on ameloblastoma.
(RGUHS, Oct. 2010)

Ans. Ameloblastoma is a true neoplasm of enamel organ type tissue which does not undergo differentiation to the point of enamel formation. It has been described as usually unicentric, nonfunctional, intermittent in growth, anatomically benign and clinically persistent.

Pathogenesis

The tumor may be derived from:

1. Cell rests of enamel organ

2. Epithelium of odontogenic cysts
3. Disturbance of developing enamel organ
4. Basal cells of the surface epithelium of jaws
5. Heterotopic epithelium in other parts of the body.

Clinical Features

1. Average age of diagnosis is 33–39 years, with wide variation.
2. No significant gender predilection
3. Mandible is the most commonly affected jaw, especially molar-angle-ramus region.
4. Usually asymptomatic, with expansion of cortices
5. Radiographically, multilocular cyst-like lesion with honeycomb and soap bubble appearance.

Treatment

Radical surgical excision.

Q. 25. Write on histological variants of ameloblastoma. (BFUHS, Nov. 2009)

Ans.

1. **Follicular ameloblastoma:** Most common variant. It is composed of many small discrete islands of tumor composed of peripheral layer of cuboidal/columnar cells.
2. **Plexiform ameloblastoma:** The cells are arranged in irregular masses, as network of interconnecting strands of cells.
3. **Acanthomatous ameloblastoma:** The cells occupying the position of stellate reticulum undergo squamous metaplasia.
4. **Granular cell ameloblastoma:** The cytoplasm of cells transforms into very coarse, granular, eosinophilic appearance.
5. **Basal cell type ameloblastoma:** Resembles to basal cell carcinoma of the skin.
6. **Desmoplastic ameloblastoma:** In this dense collagen stroma appears.

Q. 26. Describe the cysts of jaw. (TNMGR, Oct. 2012)

Ans.

a. Odontogenic cysts

i. Developmental

1. Dentigerous cyst
2. Eruption cyst
3. Odontogenic keratocyst
4. Gingival cyst of newborn
5. Gingival cyst of adult
6. Lateral periodontal cyst
7. Calcifying odontogenic cyst
8. Glandular odontogenic cyst

ii. Inflammatory

1. Periapical cyst
2. Residual cyst
3. Paradental cyst

b. Non-odontogenic cysts

1. Globulomaxillary cyst
2. Median mandibular cyst
3. Nasoalveolar cyst/nasolabial cyst
4. Palatal and alveolar cysts of newborns
5. Thyroglossal tract cyst
6. Epidermal inclusion cyst
7. Dermoid cyst
8. Heterotopic oral gastrointestinal cyst.

Q. 27. Write a short note on periapical cyst.

(TNMGR, April 2013, Oct. 2014)

Ans. It is the most common odontogenic cyst. It is the sequelae of periapical granuloma due to pulpal necrosis. It is a true cyst. The epithelium is derived from respiratory epithelium of maxillary sinus, oral epithelium of fistulous tract.

Pathogenesis

1. Proliferation of epithelial rests in the periapical area involved by granuloma.
2. The central cell becomes separated from the source of nutrition, eventually degenerate and liquefies, to form epithelium lined cavity filled with fluid.
3. The cyst further increases in size by osmosis, local fibrinolysis, and continuous epithelial proliferations.

Clinical Features

1. Most of the cysts are asymptomatic
2. Commonly seen between 20 and 60 years
3. The most commonly involved teeth are maxillary anterior.
4. The associated tooth is nonvital
5. Expansion of the cortical plates is uncommon
6. Radiographically, it appears as well defined radiolucency, surrounded by well defined radiopaque corticated border.

Treatment

Either extraction with removal of periapical tissue or root canal treatment with apicoectomy.

Q. 28. Write a short note on carcinoma of cheek.

(TNMGR, April 2000)

Ans. This constitutes 3% of oral carcinoma. It is 10 times more common in men and occurs chiefly in elderly patient.

Etiology

1. Use of chewing tobacco
2. Chewing betel nut
3. Previous leukoplakia
4. Chronic cheek biting

Clinical Features

1. Most frequently it occurs along the occlusal plane
2. The lesion is usually painful ulcer, with induration
3. The incidence of metastasis is around 45%
4. The most common sites of metastases are sub-mandibular lymph nodes.

Treatment

Either surgery or radiotherapy.

Q. 29. Write briefly about the different types of benign tumors of the jaws. (TNMGR, Oct. 2013)

Ans.

a. Odontogenic tumors

i. Epithelial

1. Ameloblastoma
2. Adenomatoid odontogenic tumor
3. Calcifying epithelial odontogenic tumors
4. Ameloblastic fibroma
5. Ameloblastic odontoma
6. Odontoma

ii. Mesodermal

1. Odontogenic myxoma
2. Odontogenic fibroma
3. Cementoma

b. Non-odontogenic tumors

1. Central fibroma
2. Myxofibroma
3. Osteoma
4. Osteoblastoma
5. Chondroma
6. Giant cell granuloma
7. Central hemangioma
8. Benign tumors of neural tissues

Fibro-osseous lesions

1. Fibrous dysplasia
2. Cherubism
3. Ossifying fibroma
4. Central giant cell granuloma.

Q. 30. Mention the white lesions of the oral cavity with their clinical features. (TNMGR, Oct. 2013)

Ans.

Classification

1. Hereditary/developmental

- a. Leukoedema
- b. White spongy nevus
- c. Hereditary benign intraepithelial dyskeratosis
- d. Pachyonychia congenital
- e. Dyskeratosis congenital

2. Reactive

- a. Frictional keratosis
- b. Morsicatio buccarum
- c. Nicotine stomatitis
- d. Tobacco pouch keratosis
- e. Chemical burn

3. Immunologic

- a. Lichen planus
- b. Lichenoid reaction
- c. Discoid lupus erythematosus
- d. Graft-versus-host disease

4. Bacterial/viral/fungal

- a. Candidiasis
- b. Mucous patches in secondary syphilis
- c. Oral hairy leukoplakia

5. Systemic disease: Uremic stomatitis

6. Potentially malignant disorders

- a. Leukoplakia
- b. Actinic cheilitis

7. Neoplastic: Squamous cell carcinoma.

Q. 31. Write a short note on theory of focal infection. (BFUHS, May 2008; HP, May 2015)

Q. Write a short note on foci of dental infection.

(RGUHS, May 2013)

Ans. A **focal infection** is a localized or generalized infection caused by the dissemination of microorganisms or toxic products from a focus of infection.

Focus of infection refers to a circumscribed area of tissue, which is infected with exogenous pathogenic microorganisms and is usually located near a mucous or cutaneous surface.

Mechanism of focal infection: There may be a metastasis of microorganism from an infected focus by either hematogenous or lymphogenous spread. Toxins or toxic products may be carried through the blood-stream or lymphatic channels from a focus to a distant site where they may incite a hypersensitive reaction.

Oral foci of infection

1. Infected periapical lesions such as the periapical granuloma, cysts, abscess.
2. Teeth with infected root canals

3. Periodontal disease
4. Bacteremia following tooth extraction/periodontal manipulation/after oral prophylaxis.

Significance of oral foci of infection: There has evidence that shows that oral foci of infection either cause or aggravate many systemic conditions.

1. Arthritis, rheumatoid and rheumatic fever type
2. Valvular heart disease, subacute bacterial endocarditis
3. Gastrointestinal diseases
4. Ocular diseases
5. Skin diseases
6. Renal diseases.

Q. 32. Write a short note on autoimmune disease.

(RGUHS, May 2013)

Ans. Autoimmune disease is a disorder in which there is evidence of an immune response against self. Auto-immune disease may be primarily due to either antibodies (autoantibodies) or immune cells, but a common characteristic is the presence of a lymphocytic infiltration in the target organ. For example, diabetes mellitus, autoimmune thyroiditis, Sjögren's syndrome, SLE, multiple sclerosis.

Etiology

1. Hidden or sequestered antigen theory, in which response is induced to an antigen that does not normally circulate in the body.
2. A response to an altered antigen
3. A response to a foreign antigen that is cross reactive to self antigen.
4. Mutation in immunocompetent cell to acquire responsiveness to self antigens.
5. Loss of immunoregulatory power by T cells.

Autoimmune Diseases

1. Systemic lupus erythematosus
2. Scleroderma
3. *Idiopathic inflammatory myopathies*: Polymyositis, dermatomyositis, myositis associated with cancer/connective tissue disorders, inclusion body myositis
4. Rheumatoid arthritis
5. Mixed connective tissue disease
6. *Vesiculoulcerative disease*: Aphthous ulcer, Behçet's disease, pemphigus, pemphigoid, dermatitis herpetiformis.
7. *Salivary gland diseases*: Sjögren's syndrome, Mikulicz's disease.
8. Pernicious anemia
9. Myasthenia gravis

10. Hashimoto's thyroiditis
11. Grave's disease.

Q. 33. What is osteomyelitis? Mention the management of body of mandible.

(BFUHS, May 2004; TNMGR, Oct. 2013)

Ans. Osteomyelitis is defined as the inflammation of bone and its marrow contents.

Predisposing Factors

1. Fracture due to trauma
2. Gunshot wounds
3. Radiation damage
4. Paget's disease
5. Osteopetrosis
6. Systemic conditions like malnutrition, acute leukemia, uncontrolled diabetes, sickle cell anemia, chronic alcoholism.

Classification

- a. **Acute**: Acute suppurative osteomyelitis
- b. **Chronic**
 - i. Chronic suppurative osteomyelitis
 - ii. Chronic focal sclerosing osteomyelitis
 - iii. Chronic diffuse sclerosing osteomyelitis
 - iv. Garre's osteomyelitis

Management

1. General principles of management include debridement, drainage and antimicrobial therapy.
2. If sequestrum is large, surgical excision.

Q. 34. Write a short note on cavernous sinus thrombosis.

(TNMGR, Oct. 2000)

Ans. Cavernous sinuses are bilateral venous channel for content of middle cranial fossa. Areas drained by cavernous sinus include orbit, paranasal sinuses, anterior mouth and middle portion of face. Cavernous sinus thrombosis is serious conditions consisting in formation of thrombus in cavernous sinus or its communicating branches. Infections of head, face, intraoral structures above the maxilla are prone to disease. There are many routes where infection may reach the cavernous sinus. The facial and angular veins carry infections from face and lip, while dental infection is carried by way of pterygoid plexus.

Clinical Features

- a. Edema of eyelids as well as chemosis
- b. Paralysis of external ocular muscles along with impairment of vision and photophobia or lacrimation.
- c. Headache, nausea, vomiting, pain, chills and fever.

Treatment

A combinations of intravenous antibiotics, anti-coagulants and surgery is optimal treatment.

Q. 35. Write a short note on pre-neoplastic conditions.

(Bangalore Uni., Jan. 1992; TNMGR, March 2002, Sept. 2010)

Q. Write a short note on leukoplakia.

(TNMGR, Oct. 2000)

Ans. Precancerous lesions are defined as a morphologically altered tissue in which cancer is more likely to occur than its apparently normal counterpart. For example, leukoplakia, erythroplakia, actinic cheilitis, palatal changes with reverse smoking.

Premalignant condition is defined as a generalized state associated with increased risk of cancer, e.g. oral submucous fibrosis, syphilis, sideropenic dysphagia, oral lichen planus, discoid lupus erythematosus, dyskeratosis congenital.

Leukoplakia: Leukoplakia is a white oral precancerous lesion with a recognizable risk for malignant transformation. Leukoplakia is currently defined as "a white patch or plaque that cannot be characterized clinically or pathologically as any other disease".

Classification

a. According to clinical description

1. Homogenous
2. Non-homogenous
3. Erythroplakia

b. According to etiology

1. Tobacco induced
2. Non-tobacco induced

c. According to risk of future development of oral cancer

1. *High risk sites:* Floor of mouth, lateral or ventral surface of tongue, soft palate.
2. *Low risks:* Dorsum of tongue, hard palate
3. *Intermediate group:* All other sites

d. According to histology

1. Dysplastic
2. Non-dysplastic

e. According to extend

1. Localized
2. Diffused

Staging of leukoplakia: In this staging three parameters are used.

Size: Denoted by L

L1—size is less than 2 cm

L2—size is in range of 2–4 cm

L3—size is more than 4 cm

L4—size is not specified

Clinical aspect: Denoted by C

C1—homogenous

C2—non-homogenous

Cx—not specified

Pathological features: Denoted by P

P1—no dysplasia

P2—mild dysplasia

P3—moderate dysplasia

P4—severe dysplasia

Px—not specified

Etiopathogenesis

a. Local factors

1. Tobacco—used in two forms

- a. Smokeless tobacco—chewable tobacco and oral use of snuff.
- b. Smoking tobacco—cigar, bidi and pipe

2. Alcohol

3. Chronic irritation

4. Candidiasis

5. Electromagnetic reaction

b. Systemic factors

1. Syphilis

2. Vitamin deficiency

3. Nutritional deficiency

4. Hormones

5. Drugs

6. Virus

Pathogenesis

Tobacco (chemical constituents and combustion products such as tars and resins), additional effect of heat from the burning of tobacco. Irritation of oral mucosa producing leukoplakic changes.

Clinical Features

a. Age—average 60 yrs

b. Sex—M : F = 3 : 2

c. Site—occur anywhere on oral mucosa. Buccal mucosa and commissure are commonly involved. Lip lesions are more common in men and tongue lesions are more common in women.

d. Small, well localized, irregular patches to diffused lesions involving oral mucosa.

- e. Surface of lesion is often finely wrinkled, may feel rough on palpation.
- f. Color may be white or yellowish white, but with heavy use of tobacco may assume brownish color.

Treatment

1. Tobacco cessation counseling
2. Topical antifungal for 2 weeks
3. Biopsy and topical vit A application
4. Beta carotene—5000 IU/day

Erythroplakia: It is defined as “any lesion of the oral mucosa that presents as a bright red velvety plaque which cannot be characterized clinically or pathologically as any other recognizable condition”.

Etiology and Pathogenesis

- a. Tobacco and alcohol are probably involved in most cases.
- b. Reverse chutta smoking is strongly associated
- c. HPV and *Candida albicans* may have a role in pathogenesis.

Clinical Presentation

It appears as a red macule or plaque with well-demarcated borders. The texture is characterized as soft and velvety. An adjacent area of leukoplakia may be found along with the erythroplakia. Occurs most frequently in older men. Most common sites for involvement are floor of mouth, lateral tongue, retro-molar pad, and soft palate.

Histopathological Diagnosis

“Epithelial dysplasia” is an entity with histologic abnormalities suggesting that the lesion has a greater probability of undergoing malignant change than does normal tissue. Hyperkeratosis is an increased thickness of the parakeratin or orthokeratin layer of the epithelium.

Treatment

1. The recommended treatment for oral lesions at high risk for malignant transformation with severe epithelial dysplasia or carcinoma *in situ* has been surgical excision of lesions with scalpel or CO₂ laser and regular follow-up examinations of lesions which histologically show no to moderate epithelial dysplasia.
2. Non surgical interventions include vitamin A, retinoid, bleomycin, mixed tea and β-carotene.

Q. 36. Write about Treacher-Collins syndrome.

(TNMGR, Sept. 2007)

Ans. Also known as mandibulofacial dysostosis. Inheritance is autosomal dominant, with males and females are equally affected.

Clinical Features

1. Anti-mongoloid palpebral fissures with coloboma of outer portion of lower lids.
2. Deficiency of eyelashes
3. Hypoplasia of facial bones
4. Malformation of external ears
5. Macrostomia
6. High palate
7. Malocclusion of teeth
8. Blind fistula between angle of ears and angle of mouth.
9. Tongue shaped process of hairline extending towards the cheeks.
10. Facial clefts and skeletal deformities
11. Characteristic bird-like or fish-like face.

Q. 37. Write about fibrous dysplasia of bone.

(TNMGR, March 2008)

Ans. Fibrous dysplasia is a skeletal developmental anomaly of the bone forming mesenchyme that manifests as a defect in osteoblastic differentiation and maturation.

Etiology

Mutation in GNAS1 gene.

Clinical Features

1. **Monostotic form:** Involvement of single bone. 70–80% fibrous dysplasia is monostotic form. This form may present with pain and pathological fracture in aged patient.
2. **Polyostotic form:** 20–30% of fibrous dysplasia involves more than one bone. Usually patient has pain in limb followed by limp.
 - i. **Jaffe's type:** Fibrous dysplasia of bones with pigmented lesions of skin or café au lait spots.
 - ii. **Albright's syndrome:** Fibrous dysplasia involving nearly all bones in the skeleton with endocrinal disturbances.
3. **Craniofacial form:** This form occurs in 10–25% cases of monostotic and 50% case of polyostotic form. The site most common involved is frontal, sphenoid, maxillary and ethmoidal bones. The other features include hypertelorism, cranial asymmetry, facial deformity, visual impairment, exophthalmos and

blindness, vestibular dysfunction, tinnitus, hearing loss, anosmia, depending upon the bone involvement.

Radiographic Features

Typical groundglass appearance.

Treatment

Conservative to prevent deformity.

Q. 38. Write a short note on trisomy 21.

(TNMGR, March 2009)

Ans. Trisomy 21 or Down syndrome is a common form of mental retardation associated with mongolism and other somatic abnormalities.

Clinical Features

1. It is the most common autosomal abnormality, occurring 1 per 700 live births.
2. Both genders are affected equally
3. Mental retardation
4. Brachycephaly
5. Hypertelorism
6. Depressed nasal bridge
7. Flat occiput
8. Broad short neck
9. Mongoloid face
10. Medial epicanthal fold
11. Strabismus
12. Ocular anomalies
13. Short stature, feet and hands
14. Clinodactyly
15. Wide gap between first and second toes

Oral Manifestations

1. Microstomia
2. Macroglossia
3. Scrotal tongue
4. Hypoplasia of maxilla
5. Delayed tooth eruption
6. Partial anodontia
7. Enamel hypoplasia
8. Juvenile periodontitis
9. Cleft lip/palate
10. Angular cheilitis
11. Geographic tongue.

Q. 39. Discuss the pathophysiology of residual ridge resorption.

(TNMGR, March 2009)

Ans. It is defined as diminishing quantity and quality of residual ridge after teeth are lost. The basic structural

change in RRR is reduction in the size of bony ridge under mucoperiosteum. It is primarily localized loss of bone structure.

Etiology of Residual Ridge Resorption

1. **Anatomic factor:** Rate of resorption of the alveolar bone depends on anatomic factors include size, shape, cortical, cancellous and density of the ridges, the thickness and character of the mucosal covering, ridge relationships number and depth of the sockets.
2. **Metabolic factors:** These are multiple nutritional and hormonal factors which influence the relative cellular activity of the bone forming cells.
3. **Functional factors:** Intensity, duration and direction of force applied are somehow translated into biologic cell activity resulting in either bone formation as bone resorption depending upon the patient's individual resistance to these forces.
4. **Dietary factors:** Abnormalities of calcium-phosphorus elements of the bloodstream are associated with alveolar resorption and rarefaction. Deficiency of vitamin A causes poor calcification of bone. Deficiency of vitamin C causes decalcification of bone and is responsible for diffuse alveolar atrophy. Deficiency of vitamin D disturbs the calcium phosphorus balance and promotes bone resorption.
5. **Prosthetic factor:** Includes various techniques, materials, concepts, principles incorporated in the prosthesis, it is desirable for a prosthesis to fit well and distribute its load over as wide area as possible, that load being kept to minimum by careful selection of tooth material and form.

Pathophysiology

It is normal function of bone to undergo constant remodeling throughout life through the processes of bone resorption and bone formation. Except during growth, when bone formation exceeds bone resorption, bone resorption and bone formation are normally in equilibrium. RRR is a localized pathologic loss of bone that is not built back by simply removing the causative factors. Yet physiologic process of internal bone remodeling goes on even in the presence of this pathologic external osteoclastic activity that is responsible of loss of bone substance. It is clear that a great deal of residual ridge may be removed in toto, and yet there is often a cortical layer of bone over the crest of the ridge. This means that new bone has been laid down inside the residual ridge in advance of the external osteoclastic removal of bone. Structurally, the configuration of endosteal bone is dependent upon the

configuration of the bony surfaces on which the inward endosteal bone growth is deposited. Thus, endosteal bone growth is dependent upon the configuration of the bony surfaces on which the inward endosteal bone growth is deposited. If endosteal bone growth fails to keep pace with the external osteoclastic activity, one would end up with an absence of a cortical layer and exposure of the medullary layer to the external surface of the bone, resulting in defects on the crest of the ridge.

Q. 40. Write a short note on long face syndrome.

(TNMGR, Oct. 2013)

Ans. Long face morphology is a relatively common presentation among orthodontic patients. Both genetic and environmental factors have been associated with the etiology of excessive vertical facial development, although it is likely that more than one subtype of the phenotype exists. Etiological factors such as enlarged adenoids, nasal allergies, weak masticatory muscles, oral habits, and genetic factors have all been implicated in the development of the long face morphology.

Clinical Features

1. Longer lower-third of the face
2. Facial retrognathism
3. Depressed nasolabial areas
4. Excessive exposure of the maxillary teeth and gingiva.
5. Lip incompetence
6. Narrow palate
7. Posterior cross-bites
8. An anterior open-bite.

Treatment

The clinician must address the three-dimensional dentoalveolar and skeletal problems that present in long face syndrome. Treatment modality depends on the growth potential of the patient when he reports as well as the severity of the dysplasia.

The two traditional methods for impeding excessive vertical growth have been

- i. High-pull headgear with maxillary fixed appliance.
- ii. A functional appliance with bite blocks.

Q. 41. Write a short note on acoustic neuroma.

Ans. It is a benign tumor of Schwann cells of the 8th cranial nerve. It may manifest as isolated case or part of neurofibromatosis 2. As isolated finding, it occurs after 3rd decade and more frequently in females. It commonly arises near the nerve's entry into the medulla or in the internal auditory meatus, usually on the vestibular division.

Clinical Features

1. Hearing loss
2. Sensory disturbances of the face
3. Vertigo
4. Ataxia
5. Cerebellar signs in the limbs
6. Hydrocephalus
7. Facial palsy after removal of tumor.

Investigations

MRI and CT

Management

Surgical removal. Prognosis is excellent.

Q. 42. Write about oral manifestations of systemic conditions of dental relevance.

(TNMGR, Sept. 2008; TNMGR, April 2015)

Ans. The mouth has been called a mirror of the body. The oral cavity provides many diagnostic clues to systemic disease and may be the first indication of a systemic condition.

a. Blood dyscrasias: The mouth may be the site of the earliest signs of blood dyscrasias. Manifestations may include hemorrhage, infection, and cellular infiltration of tissues. Diffuse gingival hypertrophy may be present in leukemia. This hypertrophy is related to infiltration of leukemic cells into the gingival tissues. Patients are predisposed to necrotic changes in tissue secondary to trauma or infection that may result in specific local complaints. Gingival bleeding or accumulation of blood in tissues may occur secondary to a platelet deficiency. Patients are predisposed to fungal infections (*Candida albicans*) and certain viral infections (herpetic stomatitis and herpes zoster) which may be the initial complaint in a blood dyscrasia. Also, medical management of leukemias may lead to secondary complications in the oral cavity. These may include secondary microbial infections, generalized oral inflammatory changes (stomatitis), and secondary bone marrow depression and related changes. Gingival hemorrhage and oozing may be evidence of thrombocytopenia. Oozing from marginal gingival tissue is common. Anemia may be due to pathosis involving the bone marrow and nutritional deficiency states. General symptoms, including fatigue, shortness of breath, and pallor, together with oral manifestations, may indicate the need for investigation. Pallor of the oral mucosa and nonspecific complaints including pain and burning may occur. Changes often involve the tongue, which may show loss of papillae.

b. Metabolic disease: Oral manifestations may result from abnormal hormonal regulation. Manifestations of diabetes frequently occur in the oral cavity. These may include dry mouth, symptoms of burning, tenderness of the mucosa, and heightened reactivity to local irritation of bacterial plaque. Clinically, the presence of infection may result in acute gingival inflammation, abscess formation, and proliferations of granulation tissue from the margins of the gums. Delayed healing and secondary infection may be present following minor trauma and oral treatments. Sex hormone imbalance can result in marked reaction to local irritations of oral tissues. This may occur during puberty, pregnancy, and with use of oral contraceptives. Changes resemble gingivitis and periodontitis, with marked inflammatory reaction to bacterial plaque present in the oral cavity. Also hyperplastic tissue responses are commonly seen, resulting in soft tissue growths on the gum tissue. Hypofunction of the adrenal cortex, resulting in Addison's disease, may present accumulation of brownish melanotic pigment in a general fashion, or as blotches in the oral soft tissue.

c. Dermatological disease: Lichen planus is a common dermatologic condition occurring in the oral cavity. Oral complaints, when present, include burning and itching. Signs and symptoms may be minimal until an ulcerative form of the condition is present. Clinically, the condition presents diagnostic white striations (Wickham's striae) and plaque-like white areas on the tissue. Inflammation adjacent to the white striations or ulceration indicates the need for treatment. Benign mucous membrane pemphigoid (BMMP) is a dermatologic condition principally affecting the gum tissues. Bullae and ulceration may occur in the oral tissues, or the condition may be relatively asymptomatic. In pemphigus, oral lesions may be the initial, and possibly the only manifestation of the condition. The sites most commonly affected are the lips, cheeks, and floor of the mouth. The mucosal surfaces are friable and will slough when subjected to minor physical irritation. The condition is relatively painless until ulceration occurs.

d. Connective tissue disease: Sjögren's syndrome is characterized by dry mouth (xerostomia), keratoconjunctivitis sicca, and other collagen diseases—often rheumatoid arthritis. Signs and symptoms related to the dry mouth may be the patient's most significant complaint. These include difficulty in chewing and mastication, altered taste sensation, difficulty with speech and denture use, rapid rate of cavities, and burning mucosa. There may also be enlargement of the salivary glands, primarily the parotid. Lesions present

with central areas of mucosal atrophy with keratotic white margins surrounded by inflammation, in an irregular distribution. Rheumatoid arthritis may affect the temporomandibular joint. Signs and symptoms include pain, clicking and grinding in the joint, limitation of jaw function, and a changing occlusion of teeth. As with other areas of arthritis, the area may appear inflamed and tender. Radiographic evidence of rheumatoid arthritis may be present.

e. Nutritional deficiencies: Due to rapid cell turnover of the oral mucosa, nutritional deficiencies may present first with oral manifestations. Changes may occur in tongue papillae, mucosal color and integrity, and in oral sensation. Vitamin B deficiencies most often appear as a general deficiency. The most common oral changes are: Inflammation and loss of tongue papillae (glossitis), a burning sensation and pain in the corners of the mouth, and generally throughout the oral cavity. Deficiency states related to the anemia (iron deficiency, folic acid deficiency and vitamin B₁₂ deficiency) may also be associated with burning of the oral mucosa, glossitis, and stomatitis. Paresthesia and abnormal peripheral nerve function may occur with vitamin B₁₂ deficiency. Lack of vitamin C (scurvy) may present with a gingival inflammation with intense reddening and frequent hemorrhage from the gums.

Q. 43. Discuss saliva—a diagnostic tool in dental diseases. (TNMGR, March 2010)

Ans. The use of saliva as a diagnostic fluid for various human ailments is gaining popularity as it offers distinct advantages over serum. These include:

1. The non-invasive nature of saliva collection
2. Simplicity of collection
3. Cost-effective for screening large populations

Whole saliva is most frequently used for diagnosis of systemic diseases since it is readily collected and contains serum constituents.

Gland-specific saliva is useful for investigating pathology of major salivary glands.

Saliva Uses

DNA: Standard genotyping

- Bacterial infection
- Diagnosing carcinomas of the head and neck
- Forensic

RNA: Viral/bacterial identification.

- Carcinomas of the head and neck.

Proteins: Diagnosing periodontitis.

- Diagnosing carcinomas of the head and neck.
- Detecting dental caries.

Mucins/glycoprotein: Diagnosing carcinomas of the head and neck.

- Detecting dental caries.

Immunoglobulin: Diagnosing viruses (HIV, hepatitis B and C).

Metabolites: Diagnosing periodontitis.

Drugs and their metabolites: Monitoring drug abuse.

- Detecting of drugs in the body.

Viruses, bacteria: Epstein-Barr virus reactivation (mononucleosis).

Cellular material: Diagnosing carcinomas of the head and neck.

1. Saliva in diagnosing autoimmune diseases: One of the most common autoimmune diseases is Sjögren's syndrome which mainly afflicts women in their 4th–5th decades. It is a chronic disease affecting the lachrymal, salivary, and other exocrine glands; viruses of the HTLV-1 play a significant role in its pathogenesis. Recently, modern methods of protein analysis demonstrated a raised level of lactoferrin, β_2 microglobulin, lysozyme c, cystatin c, and a decrease in salivary amylase and carbonic anhydrase in case of Sjögren's syndrome.

Saliva provides an ideal medium for the detection of pro-inflammatory markers of the oral cavity. In patients with oral lichen planus (OLP), TNF- α level in saliva are elevated, correlating with the severity of illness. Genetic analysis of peripheral blood has revealed differences in the metabolism of interferon in Sjögren's syndrome, systemic lupus erythematosus, dermatomyositis and psoriasis.

2. Saliva in oncological diagnostics: Saliva testing, a non-invasive alternative to serum testing, may be an effective modality for diagnosis and for prognosis prediction of oral cancer, as well as for monitoring post-therapy status, by measuring specific salivary macromolecules, examining proteomic or genomic targets such as enzymes, cytokines, growth factors, metalloproteinase's, endothelin, telomerase, cytokeratins, mRNA's and DNA transcripts. In recent years, significant alterations have been demonstrated in the saliva of oral cancer patients in the epithelial tumor markers—Cyfra 21-1, TPS and CA12, various oxidative stress-related salivary parameters as ROS and RNS, biochemical and immunological parameters as IGF and MMPs and RNA transcripts of IL8, IL-1B, DUSP1, HA3, OAZ1, S100P, and SAT. A mutation of the tumor suppressor gene p53 is common to many malignancies. Other research has been directed to detecting the human papillomavirus (HPV 16 DNA) in saliva, as one of many etiologic agents. A more recent

trend is the detection of protein markers in the diagnosis of carcinoma of the oral cavity. For example, the level of carcinoembryonic antigen (CEA) in saliva in the presence of malignancies of the oral cavity is increased, while the level of gastrointestinal cancer antigen is decreased. The level of human alphadefensin-1 (hnp-1), as a protein marker, is reduced in patients after the surgical removal of tumor. This protein marker was not detected in healthy people. Oral fluid is also used in diagnosing other malignancies.

3. Saliva in diagnosing cardiovascular disease: It is possible to detect salivary alpha-amylase as a protein biomarker using chromatography or immune-analysis. The latest studies report raised activity of salivary alpha-amylase connected to stress in adolescents.

4. Saliva for diagnostic testing of medicines and drugs: Diagnostic testing of drugs and prescription medicines using saliva/oral fluid is now widespread and replacing the previously used urine. Certain drugs such as amphetamines and cocaine appear in saliva before they do in plasma owing to their acidity. Generally, it can be said that the level of drugs, medicines, or their metabolites remain in saliva from a number of hours up to days after their intake. Most recently, law enforcement agencies have employed saliva-based tests for roadside evaluation of alcohol levels and in hospital emergency departments as a rapid means of determining whether impaired consciousness is related to alcohol intoxication. Monitoring levels of salivary nicotine has proven useful in monitoring self-reported compliance with smoking cessation programs.

5. Infectious disease: Saliva is superior to serum and urine to both sensitivity and specificity in testing for HIV infection, human herpesvirus, cytomegalovirus, Epstein-Barr virus, hepatitis C virus. Saliva contains immunoglobulins (Ig) that originate from two sources: The salivary glands and serum. The predominant Ig in saliva is secretory IgA (sIgA), which is derived from plasma cells in the salivary glands, salivary IgM and IgG are primarily derived from serum via GCF, and are present in lower concentrations in saliva than is IgA. Antibodies against viruses and viral components can be detected in saliva and can aid in the diagnosis of acute viral infections, congenital infections, and reactivation of infection. Salivary IgA levels to HIV decline as infected patients become symptomatic.

6. Saliva and wound healing: Salivary EGF speeds up the healing process by its angiogenetic and cell proliferating effects. Other growth factors present in saliva such as transforming growth factor- β , fibroblast growth factor, insulin-like growth factors and nerve

growth factor also contribute to the healing process. Furthermore, saliva contains several blood clotting factors (IXa, VIII, XI) at a level comparable to plasma, and saliva can replace platelets in the thrombin generation.

7. Oral diseases: Evaluation of the quantity of whole saliva is simple and may provide information, which has systemic relevance. **Quantitative alterations** in saliva may be a result of medications. At least 400 drugs may induce xerostomia and may lead to oral problems like progressive dental caries, fungal infection, oral pain, and dysphagia. **Qualitative changes** in salivary composition can also provide diagnostic information concerning oral problems: Increased levels of albumin in whole saliva were detected in patients who received chemotherapy as treatment for cancer and subsequently developed stomatitis, reduced salivary EGF levels may be important for the progression of radiation-induced mucositis, higher levels of salivary nitrate and nitrite, and increased activity of nitrate reductase were found in oral cancer patients. Saliva is also very suitable for the monitoring of oral bacteria that can survive in saliva, and can utilize salivary constituents as a growth medium, for example, increased numbers of *Streptococcus mutans* and Lactobacilli in saliva were associated with increased caries prevalence and with the presence of root caries, detection of certain bacterial species in saliva can reflect their presence in dental plaque and periodontal pockets. The changes of the components of the saliva may also be used for periodontal diagnosis. Recent studies focus on the potential role of periodontal disease as a risk factor for cardiovascular and cerebrovascular diseases as a possible link with metabolic syndrome and oxidative stress.

Saliva and xerostomia: In healthy humans, the resting flow rate is around 1 ml/min. Xerostomia usually appears when resting unstimulated whole saliva flow rate is less than 0.1–0.2 ml/min and stimulated flow rate is less than 0.4–0.7 ml/min. In other cases (25% of patients), the resting flow rate decreases, but the stimulated flow remains normal. In other patients (22%), both resting and stimulated flow rate is normal. In serious cases, saliva demonstrates low pH and buffer capacity, increased total protein albumin and sodium concentration, decreased amylase/protein ratio, and high lactobacillus and yeast concentration. The concentrations of MUC5B and MUC7 type mucins are also decreased.

Oral fluid nanosensor test: The envisioned product is called the Oral Fluid NanoSensor Test (OFNASET). The OFNASET is a handheld, automated, easy-to-use integrated system that will enable simultaneous and

rapid detection of multiple salivary protein and nucleic acid targets. This salivary biomarker detector can be used for point-of-care disease screening and detection. The salivary proteome presents one such resource. The UCLA laboratory recently discovered that discriminatory and diagnostic human mRNAs are present in the saliva of healthy people and people with disease. The salivary transcriptome offers an additional valuable resource for disease diagnostics. The behavior of these salivary transcriptome biomarkers is consistent—that is, their levels are significantly higher in the saliva of patients with oral cancer than in the saliva of matched control subjects.

Advantages of transcriptome markers: Salivary transcriptome offers the combined advantages of high throughput marker discovery via a non-invasive bio-fluidic method and high patient compliance. Highly diagnostic salivary RNA signatures have been identified for oral cancer and for two other major human systemic diseases. Recent evidence regarding saliva as a diagnostic tool for diseases such as HIV, various forms of cancer, diabetes, arthritis and heart disease has shown that much more information is contained in saliva than was previously thought.

Q. 44. Write a short note on dental management of patient with decreased salivation.

(RGUHS, November 2011)

Ans.

- 1. Preventive therapy:** Supplemental fluoride, meticulous oral hygiene, frequent dental visit, brushing after meals, remineralizing solutions, noncariogenic diet.
- 2. Symptomatic treatment:** Frequent use of water and other fluids, increased humidification, minimize caffeine and alcohol.
- 3. Local salivary stimulation:** Sugar free gums to promote chewing, electrical stimulation with low voltage current to the tongue and palate, use of acupuncture needles in the perioral region.
- 4. Systemic salivary stimulation:** Pilocarpine (5 mg), cevimeline (30 mg).
- 5. Treatment of underlying systemic disorder.**

Q. 45. Write a short note on Garre's osteomyelitis.

(TNMGR, March 2007)

Ans. Distinctive type of chronic osteomyelitis in which focal gross thickening of periosteum, with peripheral reactive bone formation resulting from mild irritation or infection. It is essentially a periosteal osteosclerosis analogous to endosteal sclerosis of chronic focal and diffused sclerosing osteomyelitis.

Clinical Features

- Occur commonly below 30 years
- Males are commonly affected than females
- Frequently involves anterior surface of tibia and femur.
- Mandible is affected commonly than maxilla
- It occurs at inferior border of mandible, in first molar region.
- It is presented as hard nontender swelling with medial and lateral expansion of jaw.
- Size varies from 1 to 2 cm to involvement of entire length on affected side.
- It may become secondarily affected cause discomfort.

Radiographic Features

- Intraoral radiograph will reveal a carious tooth opposite the hard bony mass.
- Shadow of convex bone over cortex may be seen
- No trabecular pattern between shell of new bone and cortex.
- As infections persists, the cortex thickness and become laminated with altering radiopaque and radiolucent layers (onion skin appearances).

Histopathological Features

The supracortical and subperiosteal mass is composed of much reactive new bone and osteoid tissue, with osteoblasts bordering many of trabeculae. These trabeculae often perpendicular to cortex, with trabeculae arranged parallel to each other or show retiform pattern. The connective tissue between bony sprinkling of lymphocytes and plasma cells. The periosteal reaction is result of infection from carious tooth perforating its usually as attenuated, stimulating the periosteum.

Differential Diagnosis

- Ewing's sarcoma
- Caffey's disease
- Fibrous dysplasia
- Osteosarcoma

Treatment

Endodontically treated or removal of carious infected tooth with no surgical intervention for periosteal lesion.

Q. 46. Write a short note on osteoradionecrosis.

(TNMGR, March 2008)

Ans. Osteoradionecrosis is a radiation induced pathologic process characterized by a chronic and painful infection and necrosis accompanied by late sequestration and sometimes, permanent deformity.

Etiopathogenesis

Three factors are involved in the pathogenesis are radiation, trauma, and infection. Radiations cause a proliferation of the intima of blood vessels, leading to thrombosis of end arteries. This results in non-vital bone. Infection gains entry to the bone following traumatic injury, extraction, pulpal pathologies or even periodontitis. The altered bone becomes hypoxic, hypovascular and hypocellular (**3H**). The necrotic bone may undergo sequestration; this process may extend throughout the radiated bone.

Clinical Manifestations

- Mandible is affected more frequently than maxilla, because of difference in the blood supply.
- There is necrosis of bone with sequestration formation in long standing cases.
- Patient usually suffers from intense bone pain.
- There may be cortical perforation with sinus/fistula formation.
- Surface ulceration and pathological fractures also occurs eventually.
- Affected areas of bone reveals ill defined areas of radiolucency with areas of radiopacity.

Bone necrosis profile: More the factors present, greater the chance of development of necrosis.

- Irradiation of surgically treated areas, without proper healing.
- Irradiation of lesions in proximity to bone
- High dose of radiation without proper fractionation
- Poor oral hygiene
- Poor patient cooperation in managing irradiated tissues.
- Surgery in irradiated areas
- Inappropriate use of prosthesis after radiation therapy.
- Failure to prevent trauma to irradiated bony areas
- Presence of physical and nutritional problems.

Q. 47. Write a short note on syndromes related to maxillofacial region. (TNMGR, March 2010)

Ans. A pattern of multiple anomalies pathogenetically related but not representing a single sequence or developmental field.

Syndrome Related to Maxillofacial Region

a. Syndrome of developmental disturbances during growth

- Cleft lip/palate
- Parry Romberg syndrome
- Vander Woude's syndrome

4. Ascher's syndrome
 5. Orofacial digital syndrome
 6. Median cleft face syndrome
 7. Meischer's syndrome
 8. Melkersen-Rosenthal syndrome
 9. Branchial arch syndrome
 10. Peutz-Jeghers syndrome
 11. Rubinstein-Taybi syndrome
 12. Klinefelter's syndrome
 13. Gardner's syndrome
- b. Syndrome related to benign and malignant tumors**
1. Cowden's syndrome
 2. B-K mole syndrome
 3. Multiple endocrine neoplasia syndromes
 4. Sipple syndrome
- c. Syndrome related to salivary gland: Sjögren's syndrome.**
- d. Syndrome of odontogenic cysts and tumors: Gorlin-Goltz syndrome.**
- e. Syndrome related to infections**
1. Heerfordt's syndrome
 2. Behçet's syndrome
 3. Reiter's syndrome
 4. Ramsay Hunt syndrome
- f. Syndromes related to bone and joints**
1. Albright's syndrome
 2. Crouzan syndrome
 3. Apert syndrome.
 4. Treacher-Collins syndrome/mandibulofacial dysostosis/Franchetti syndrome
 5. Pierre-Robin syndrome
 6. Marfan syndrome
 7. Down syndrome (trisomy 21)
 8. Van Buchem syndrome
 9. Gorham syndrome
 10. Albright syndrome
 11. Caffey-Silverman syndrome
 12. Costen syndrome
 13. Myofascial pain dysfunction syndrome
 14. Maffucci's syndrome
- g. Syndrome related to blood**
1. Fanconi syndrome
 2. Plummer-Vinson syndrome
 3. Aldrich syndrome
 4. Chédiak-Higashi syndrome
 5. Kostmann syndrome
- h. Syndrome related to skin diseases**
1. Stevens-Johnson syndrome
 2. Crest syndrome

3. Ehlers-Danlos syndrome
 4. Papillion Lefebvre syndrome
- i. Syndromes related to neuromuscular system**
1. Reader's syndrome
 2. Frey's syndrome
 3. Horner's syndrome
 4. Jaw-winking syndrome
 5. Trotter's syndrome
 6. Eagle's syndrome
 7. Floppy infant syndrome
 8. Mobius syndrome
 9. Horton's syndrome
- j. Syndrome related to metabolic disorders**
1. Cushing's syndrome
 2. Hurler's syndrome
 3. Hunter's syndrome
 4. Waterhouse-Friederichsen syndrome.

Q. 48. Write a short note on sialadenitis.

(TNMGR, Oct. 2011)

Ans.

- a. Allergic sialadenitis:** Enlargement of the salivary glands has been associated with exposure to various pharmaceutical agents and allergens. The characteristic feature of such an allergic reaction is acute salivary gland enlargement, often accompanied by itching over the gland. Compounds have salivary gland enlargement as a potential side effect include phenobarbital, phenothiazine, ethambutol, sulfisoxazole, iodine compounds, isoproterenol, and heavy metals. Allergic sialadenitis is self-limiting.
- b. Bacterial sialadenitis:** Bacterial infections of the salivary glands are most commonly seen in patients with reduced salivary gland function. This condition was formerly referred to as "surgical parotitis" because post-surgery patients often experienced gland enlargement from ascending bacterial infection. Markedly decreased salivary flow during anesthesia, often as the result of administered anticholinergic drugs and relative dehydration due to restricted fluids. With the administration of prophylactic antibiotics and routine peri-operative hydration, this condition now occurs much less frequently.

Clinical Presentation

Sudden onset of unilateral or bilateral salivary gland enlargement. Approximately 20% of the cases present as bilateral infections. The involved gland is painful, indurated, and tender to palpation. The overlying skin may be erythematous. A purulent discharge may be

expressed from the duct orifice, and samples of this exudates should be cultured for aerobes and anaerobes. A second specimen should be sent for testing with Gram's stain. The most commonly cultured organisms include coagulase—positive *Staphylococcus aureus*, *Streptococcus viridans*, *Streptococcus pneumoniae*, *Escherichia coli*, and *Haemophilus influenzae*. Due to the dense capsule surrounding the salivary glands, it is difficult to determine, based on physical examination alone, whether an abscess has formed. Ultrasonography or CT is recommended for visualizing possible cystic areas.

Treatment

- If a purulent discharge is present, empiric intravenous administration of a penicillinase resistant anti-staphylococcal antibiotic is indicated.
- Patients should be instructed to “milk” the involved gland several times throughout the day. Increased hydration and improved oral hygiene are required.
- With these measures, significant improvement should be noted within 24 to 48 hours. If this does not occur, then incision and drainage should be considered.
- Viral sialadenitis:** It occurs in mumps. This produces pain on mastication, followed by firm, rubbery swelling of salivary glands. Treatment is conservative, maintenance of hydration.
- Sialadenitis due to mechanical obstruction:** It may occur due to sialolith in the duct or gland itself. Symptoms depend upon the site of obstruction and chronicity and the size of the sialolith. Treatment is removal of sialolith.

Q. 49. Write a short note on thyroglossal duct cyst.

Ans. The median lobe of thyroid gland develops at about fourth week of intrauterine life from a site at base of tongue which is recognized as foramen caecum. A hollow epithelial stalk known as thyroglossal cyst. It extends caudally and passes ventral to hyoid bone to ventral aspect of thyroid cartilage where it joins the developing lateral lobe. The thyroglossal duct disintegrates by tenth week, but cyst may form from residue of duct at any point along its line of descent.

Pathogenesis

Inflammatory conditions which may lead to reactive hyperplasia of lymphoid tissue adjacent to remnants of thyroglossal tract stimulate epithelial remnants themselves leading to. Thyroglossal duct with accumulation of secretion.

Clinical Features

It is common in females. Occur commonly in first, second and third decades of life. It is most commonly located in area of hyoid bone. Pain may occur if cyst is infected. If it is located high in the tract it may cause dyspnea. Cyst size may vary from 0.5 to 5 cm in diameter. It may be spherical, oval with long axis along with thyroglossal tract. It may lift when patient swallow or protrudes the tongue. Cyst usually in midline and produce softer, movable sometime fluctuant or tender swellings. Consistency is firm or hard depending upon tension of fluid within cyst.

Histopathological Features

It lined by pseudostratified columnar epithelium which may be ciliated or stratified squamous epithelium. Connective tissue wall of cyst contains small patches of lymphoid tissue, thyroid tissue and mucous gland.

Differential Diagnosis

- Subhyoid bursal cyst
- Sublingual dermoid

Management

- Surgical excision is treatment of thyroglossal duct cyst.
- Sistrunk operation involves removal of 1 cm block of tissue surrounding the duct. Duct should be traced down to pyramidal lobe of thyroid gland and foramen caecum at base of tongue.

Q. 50. Write a short note on obstructive sleep apnea. (RGUHS, May 2012; KUHS, January 2014)

Ans. Obstructive sleep apnea (OSA) is a sleep-related breathing disorder that involves a decrease or complete halt in airflow despite an ongoing effort to breathe. It occurs when the muscles relax during sleep, causing soft tissue in the back of the throat to collapse and block the upper airway. Most pauses last between 10 and 30 seconds, but some may persist for one minute or longer. This can lead to abrupt reductions in blood oxygen saturation, the brain responds to this by causing a brief arousal from sleep that restores normal breathing.

A common measurement of sleep apnea is the *apnea-hypopnea index* (AHI). This is an average that represents the combined number of apneas and hypopneas that occur per hour of sleep.

Prevalence: OSA can occur in any age group, but prevalence increases between middle and older age. About 80 percent to 90 percent of adults with OSA remain undiagnosed. OSA occurs in about two percent of children and is most common at preschool ages.

Types

1. **Mild OSA:** AHI of 5–15: Involuntary sleepiness during activities that require a little attention, such as watching TV or reading.
2. **Moderate OSA:** AHI of 15–30: Involuntary sleepiness during activities that require some attention, such as meetings or presentations.
3. **Severe OSA:** AHI of more than 30: Involuntary sleepiness during activities that require more active attention, such as talking or driving.

Risk groups: People who are **overweight** and **obese**; with **large neck sizes**; **middle-aged** and **older** men, and **postmenopausal** women; **ethnic** minorities; People with **abnormalities** of the bony and soft tissue structure of the head and neck; Adults and children with **Down syndrome**; Children with **large tonsils** and **adenoids**; Anyone who has a **family member** with OSA; People with endocrine disorders such as **acromegaly** and **hypothyroidism**; **Smokers**; those suffering from nocturnal nasal congestion due to **abnormal morphology**, **rhinitis** or both.

Effects

1. Fluctuating oxygen levels
2. Increased heart rate
3. Chronic elevation in daytime blood pressure
4. Increased risk of stroke
5. Higher rate of death due to heart disease
6. Impaired glucose tolerance and insulin resistance
7. Impaired concentration
8. Mood changes
9. Increased risk of being involved in a deadly motor vehicle accident.
10. Disturbed sleep of the bed partner.

Treatments

Sleep apnea must first be diagnosed at a sleep center or lab during an overnight sleep study, or "polysomnogram." The sleep study charts vital signs such as brain waves, heartbeat and breathing.

1. **Continuous positive airway pressure (CPAP):** CPAP is the standard treatment option for moderate to severe cases of OSA and a good option for mild sleep apnea. CPAP provides a steady stream of pressurized air to patients through a mask that they wear during sleep. This airflow keeps the airway open, preventing pauses in breathing and restoring normal oxygen levels.
2. **Oral appliances:** An oral appliance is an effective treatment option for people with mild to moderate OSA who either prefer it to CPAP or are unable to successfully comply with CPAP therapy.

3. **Surgery:** Surgery is a treatment option for OSA when noninvasive treatments such as CPAP or oral appliances have been unsuccessful.
4. **Behavioral changes:** Weight loss benefits many people with sleep apnea, and changing from back-sleeping to side-sleeping may help those with mild cases of OSA.
5. **Over-the-counter remedies:** External nasal dilator strips, internal nasal dilators, and lubricant sprays may reduce snoring.
6. **Position therapy:** A treatment used for patients suffering from mild OSA. Patients are advised to stay off of the back while sleeping and raise the head of the bed to reduce symptoms.

Q. 51. Discuss about prions in dentistry.

(TNMGR, April 2012)

Ans. Spongiform encephalopathy, also called Creutzfeldt-Jakob disease (CJD) or mad-cow disease, is caused by accumulation of prion proteins. Prion proteins are a modified form of normal structural proteins present in the mammalian CNS and are peculiar in two respects: They lack nucleic acid (DNA or RNA), and they can be transmitted as an infectious proteinaceous particles. Methods of transmission are by iatrogenic route (e.g. by tissue transplantation from an infected individual) and by human consumption of BSE (bovine spongiform encephalopathy)-infected beef, also called as mad-cow disease. Clinically, CJD is characterized by rapidly progressive dementia with prominent association of myoclonus. CJD is invariably fatal

Oral manifestations: Oral manifestations are rarely seen in prion diseases.

1. Dysphagia (difficulty in swallowing)
2. Dysarthria (poor articulation of speech). Both occur as a consequence of pseudobulbar paralysis.
3. Paresthesia (tingling, pricking or numbness)
4. Orofacial dysesthesia (abnormal sensations in the absence of stimulation)
5. Loss of taste and smell

There are two possible mechanisms assessed for the transfer of CJD via dental instruments

- a. Accidental abrasion of lingual tonsil during dental procedures. Such a chance is extremely low (10^4 - 10^9 times less likely than tonsillectomy).
- b. Contact of dental instruments with pulp tissue. As dental pulp originates from richly innervated neural crest cells, it is theoretically possible that the dental pulp of individuals infected with CJD may be infectious.

General Recommendations for Dentists

The role of the dentist is to identify the patients with different forms of Creutzfeldt-Jakob disease (CJD) and to take appropriate measures to reduce the possible risk of cross contamination. This can be achieved by obtaining: (a) complete medical history of the patient, (b) family history of prion diseases, (c) travel history to know about the possible exposure during visits to endemic areas like the United Kingdom.

Prion Inactivation Methods

The routine physical and chemical sterilizing procedures are ineffective against prion agents, as they are heat resistant and bind tightly to surgical steel instruments.

It is advisable to use disposable instruments whenever possible and incinerate reusable instruments that are difficult to clean (endodontic files, broaches, carbide and diamond burs and dental matrix bands).

The nondisposable instruments should be mechanically cleaned and passed thorough stringent decontamination protocols before reuse, as recommended by WHO.

The handling of instruments depends on the risk of the patient being treated. When treating high-risk patients, all materials must be incinerated.

The source of refrigeration and aspiration system should be external to the equipment due to the possibility that some residues might pass via internal systems and compromise sterilization.

The patient should never use the normal spittoon but a disposable receptacle that is later incinerated.

The histological samples of high-risk patients must be handled by specialized staffs that are aware of the risk. As routine formalin fixation does not inactivate prion proteins, the samples must be immediately immersed in 98% formic acid for 1 h prior to paraffin embedding and labeled as biohazardous.

In patients with suspicion of CJD, all the instruments must be stored separately in a rigid container labeled with data of the patient, type of treatment provided and details of the attending clinician until a definitive diagnosis is arrived.

The instruments are incinerated if the diagnosis is confirmed or sterilized by conventional methods like autoclaving if diagnosis is ruled out.

Dental unit waterlines must not be activated.

7. DISEASES OF BLOOD AND NUTRITIONAL DISEASES

Q. 1. Write a short note on scurvy.

(TNMGR, Sept. 2007)

Ans. Vitamin C exists in natural sources as L-ascorbic acid closely related to glucose. The major sources of vitamin C are citrus fruits such as orange, lemon, grapefruit and some fresh vegetables like tomatoes and potatoes. It is present in small amounts in meat and milk. The vitamin is easily destroyed by heating so that boiled or pasteurized milk may lack vitamin C. It is readily absorbed from the small intestine and is stored in many tissues, most abundantly in adrenal cortex.

1. Vitamin C has antioxidant properties and can scavenge free radicals.
2. Ascorbic acid is required for hydroxylation of proline to form hydroxyproline which is an essential component of collagen.
3. It is necessary for the ground substance of other mesenchymal structures such as osteoid, chondroitin sulfate, dentin and cement substance of vascular endothelium.
4. Vitamin C being a reducing substance has other functions such as hydroxylation of dopamine to norepinephrine; maintenance of folic acid levels by preventing oxidation of tetrahydrofolate; and role in iron metabolism in its absorption, storage and keeping it in reduced state.

Vitamin C deficiency in the food or as a conditioned deficiency results in scurvy. The lesions and clinical manifestations of scurvy are seen more commonly at two peak ages: In early childhood and in the very aged. These are:

1. **Hemorrhagic diathesis:** A marked tendency of bleeding is characteristic of scurvy. This may be due to deficiency of intercellular cement which holds together the cells of capillary endothelium. There may be hemorrhages in the skin, mucous membranes, gums, muscles, joints and underneath the periosteum.
2. **Skeletal lesions:** These changes are more pronounced in growing children. The most prominent change is the *deranged formation of osteoid matrix and not deranged mineralization*. The epiphyseal ends of growing long bones have cartilage cells in rows which normally undergo provisional mineralization. But, due to vitamin C deficiency, the next step of lying down of osteoid matrix by osteoblasts is poor and results in failure of resorption of cartilage. Consequently, mineralized cartilage under the widened and irregular epiphyseal plates project as **scorbutic rosary**.
3. **Delayed wound healing:** There is delayed healing of wounds in scurvy due to following: deranged collagen synthesis; poor preservation and maturation of fibroblasts; and localization of infections in the wounds.

4. **Anemia:** Anemia is common in scurvy. It may be the result of hemorrhage, interference with formation of folic acid or deranged iron metabolism.
5. **Lesions in teeth and gums:** Scurvy may interfere with development of dentin. The gums are soft and swollen, may bleed readily and get infected commonly.
6. **Skin rash:** Hyperkeratotic and follicular rash may occur in scurvy.

Q. 2. Write a short note on bleeding disorders.

(TNMGR, March 2008)

Ans. Bleeding disorders or hemorrhagic diatheses are a group of disorders characterized by defective hemostasis with abnormal bleeding. The tendency to bleeding may be spontaneous in the form of small hemorrhages (e.g. petechiae, purpura, ecchymoses), or there may be excessive external or internal bleeding (e.g. hematoma, hemarthroses, etc). The causes of hemorrhagic diatheses may or may not be related to platelet abnormalities. These causes are broadly divided into the following groups:

- i. Hemorrhagic diathesis due to vascular abnormalities.
- ii. Hemorrhagic diathesis related to platelet abnormalities.
- iii. Disorders of coagulation factors
- iv. Hemorrhagic diathesis due to fibrinolytic defects
- v. Combination of all these.

Investigations of Hemostatic Function

- a. Comprehensive clinical evaluation, including the patient's history, family history and details of the site, frequency and character of haemostatic defect.
- b. Screening tests.
- c. Specific tests.

a. Investigation of disordered vascular hemostasis

1. **Bleeding time:** Normal range is 3–8 minutes. A prolonged bleeding time may be due to the following causes:
 - i. Thrombocytopenia
 - ii. Disorders of platelet function
 - iii. von Willebrand's disease
 - iv. Vascular abnormalities (e.g. in Ehlers-Danlos syndrome)
 - v. Severe deficiency of factor V and XI
2. **Platelet count:** Thrombocytopenia.
3. **Prothrombin time:** Evaluation of extrinsic and common pathway. It is prolonged in
 - i. Oral anticoagulant therapy
 - ii. DIC

- iii. Liver disease

4. Partial thromboplastin time

- i. Parenteral heparin therapy
- ii. DIC
- iii. Liver disease

5. Thrombin time: Evaluation of common pathway.

- i. Afibrinogenemia
- ii. DIC
- iii. Parenteral heparin therapy

b. Hemorrhagic diatheses due to vascular disorders:

They are characterized by petechiae, purpura or ecchymoses. Vascular bleeding disorders may be inherited or acquired.

a. Inherited vascular bleeding disorders

1. Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease)
2. Marfan's syndrome, Ehlers-Danlos syndrome and pseudoxanthoma elasticum.

b. Acquired vascular bleeding disorders

1. Henoch-Schönlein purpura
2. Hemolytic-uremic syndrome.
3. Devil's pinches—easy bruising of unknown cause.
4. Infection
5. Drug reactions
6. Steroid purpura
7. Senile purpura
8. Scurvy

c. Hemorrhagic diatheses due to platelet disorders

- a. Thrombocytopenia
- b. **Thrombocytosis:** Platelet count in excess of 4,00,000/ μ l. It may occur in myeloproliferative disorders, following massive hemorrhage, iron deficiency, severe sepsis, marked inflammation, disseminated cancers, hemolysis, or following splenectomy.
- c. **Disorders of platelet functions:** Prolonged bleeding time but a normal platelet count.
 - i. Hereditary disorders: Bernard-Soulier syndrome, von Willebrand's disease, Glanzmann's disease.
 - ii. Acquired disorders: Aspirin therapy, uremia, liver disease, multiple myeloma, Waldenström's macroglobulinemia and various myeloproliferative disorders.

Q. 3. Write a short note on iron deficiency anemia.

(TNMGR, March 2008, 2011; RGUHS, Oct. 2010)

Ans. The commonest nutritional deficiency disorder present throughout the world is iron deficiency. Iron

deficiency anemia is always secondary to an underlying disorder.

Etiology

a. Increased blood loss

1. *Uterine*: For example, excessive menstruation, repeated miscarriages, postmenopausal uterine bleeding.
2. *Gastrointestinal*: For example, peptic ulcer, hemorrhoids, hookworm infestation, ulcerative colitis.
3. Renal tract, e.g. hematuria, hemoglobinuria
4. Nose, e.g. repeated epistaxis
5. Lungs, e.g. hemoptysis

b. Increased requirements

1. Spurts of growth in infancy, childhood and adolescence.
2. Prematurity
3. Pregnancy and lactation

c. Inadequate dietary intake

1. Poor economic status
2. Anorexia, e.g. in pregnancy
3. Elderly individuals due to poor dentition, apathy and financial constraints.

d. Decreased absorption

1. Partial or total gastrectomy
2. Achlorhydria
3. Intestinal malabsorption such as in celiac disease.

Clinical Features

1. Iron deficiency anemia is much more common in women between the age of 20 and 45 years; at periods of active growth in infancy, childhood and adolescence; and is also more frequent in premature infants.
2. All the features of the underlying disorder causing the anemia.
3. The usual symptoms are weakness, fatigue, and dyspnea on exertion, palpitations and pallor of the skin, mucous membranes and sclera. Older patients may develop angina and congestive cardiac failure. Patients may have unusual dietary cravings such as pica. Menorrhagia is a common symptom in iron deficient women.
4. Long-standing chronic iron deficiency anemia causes epithelial tissue changes in some patients. The changes occur in the nails (**koilonychia**s or spoon-shaped nails), tongue (**atrophic glossitis**), mouth (**angular stomatitis**), and esophagus causing dysphagia from development of thin, membranous

webs at the postcricoid area (**Plummer-Vinson syndrome**).

Treatment

1. Correction of the underlying disorder.

2. Correction of iron deficiency

- i. *Oral therapy*: Iron deficiency responds very effectively to the administration of oral iron salts such as ferrous sulfate, ferrous fumarate, ferrous gluconate and polysaccharide iron. The response to oral iron therapy is observed by reticulocytosis which begins to appear in 3–4 days with a peak in about 10 days.
- ii. *Parenteral therapy*: Parenteral iron therapy is indicated in cases who are intolerant to oral iron therapy, in GIT disorders such as malabsorption, or a rapid replenishment of iron stores is desired such as in women with severe anemia a few weeks before expected date of delivery. Total dose is calculated by a simple formula by multiplying the grams of hemoglobin below normal with 250 (250 mg of elemental iron is required for each gram of deficit hemoglobin), plus an additional 500 mg is added for building up iron stores. A common preparation is iron dextran. The adverse effects with iron dextran include hypersensitivity or anaphylactoid reactions, hemolysis, hypotension, circulatory collapse, and vomiting and muscle pain. Newer iron complexes such as sodium ferric gluconate and iron sucrose have much lower side effects.

Q. 4. Write a short note on megaloblastic anemia.

(TNMGR, Sept. 2009)

Ans. The megaloblastic anaemias are disorders caused by impaired DNA synthesis and are characterized by delayed maturation of nucleus than of cytoplasm in the hematopoietic precursors in the bone marrow. The underlying defect for the asynchronous maturation of the nucleus is defective DNA synthesis due to deficiency of vitamin B₁₂ (cobalamin) and/or folic acid (folate). Other causes include drugs which interfere with DNA synthesis, acquired defects of hematopoietic stem cells.

Clinical Features

1. **Anaemia**: Macrocytic megaloblastic anemia
2. **Glossitis**: Smooth, beefy, red tongue
3. **Neurologic manifestations**: Numbness, paresthesia, weakness, ataxia, poor finger coordination and diminished reflexes.

4. Others: Mild jaundice, angular stomatitis, purpura, melanin pigmentation, symptoms of malabsorption, weight loss and anorexia.

1. Laboratory findings

a. General laboratory investigations of anemia which include blood picture, red cell indices, bone marrow findings, and biochemical tests.

- i. *Hemoglobin:* Hemoglobin estimation reveals values below the normal range.
- ii. *Red cells:* Red blood cell morphology in a blood film shows the characteristic macrocytosis. In addition, the blood smear demonstrates marked anisocytosis, poikilocytosis and presence of macro-ovalocytes.
- iii. *Reticulocyte count:* The reticulocyte count is generally low.
- iv. *Absolute values:* The red cell indices reveal an elevated MCV (above 120 fl), elevated MCH (above 50 pg) and normal or reduced MCHC.
- v. *Leukocytes:* Presence of characteristic hyper-segmented neutrophils in the blood film should raise the suspicion of megaloblastic anemia.
- vi. *Platelets:* Platelet count may be moderately reduced in severely anemic patients.

2. Bone marrow findings: Hypercellular, decreased myeloid-erythroid ratio, erythroid hyperplasia. Megaloblasts are abnormal, large, having nuclear-cytoplasmic asynchrony. The nuclei are large, having fine, reticular and open chromatin that stains lightly. Increase in the number and size of iron granules in the erythroid precursors and chromosomal abnormalities.

3. Biochemical findings: Rise in serum unconjugated bilirubin and LDH, serum iron and ferritin may be normal or elevated.

b. Special tests for cause of specific deficiency

1. *Tests for vitamin B₁₂ deficiency:* Serum vitamin B₁₂ assay, Schilling (24-hour urinary excretion) test and serum enzyme levels.
2. *Tests for folate deficiency:* Urinary excretion of FIGLU, serum and red cell folate assay.

Treatment

Hydroxycobalamin (1000 µg) as IM injection for 3 weeks and oral folic acid 5 mg tablets daily for 4 months.

Q. 5. Write a short note on polymorphonuclear neutrophil (PMN) defects.

(Sumandeep Vidyapeeth, April 2011;
TNMGR, April 2014)

Ans. A polymorphonuclear neutrophil (PMN), commonly called polymorph or neutrophil, is 12–15 µm

in diameter. It consists of a characteristic dense nucleus, having 2–5 lobes and pale cytoplasm containing numerous fine violet-pink granules. These lysosomal granules contain several enzymes and are of 2 types:

1. **Primary or azurophilic granules:** Hydrolases, elastase, myeloperoxidase, cathepsin-G, defensins.
2. **Secondary or specific granules:** Lactoferrin, NADPH oxidase, histaminases.

Pathologic Variations

a. Neutrophil leukocytosis

1. Acute infections, e.g. actinomycosis, poliomyelitis, abscesses, furuncles, carbuncles, tonsillitis, otitis media, osteomyelitis, etc.
2. Other inflammations. e.g. burn, operations, collagen-vascular diseases, hypersensitivity reactions, etc.
3. Intoxication, e.g. uremia, poisonings by chemicals and drugs
4. Acute hemorrhage
5. Acute hemolysis
6. Disseminated malignancies
7. Myeloproliferative disorders, e.g. myeloid leukemia, polycythemia vera, myeloid metaplasia.
8. Miscellaneous, e.g. following corticosteroid therapy, idiopathic neutrophilia.

b. Neutropenia

1. Certain infections, e.g. typhoid, paratyphoid, measles, viral hepatitis, malaria, etc.
2. Overwhelming bacterial infections especially in patients with poor resistance, e.g. miliary tuberculosis, septicemia.
3. Drugs, chemicals and physical agents which induce aplasia of the bone marrow cause neutropenia, e.g. antimetabolites and antihistaminics.
4. Certain hematological and other diseases, e.g. pernicious anemia, aplastic anemia, cirrhosis of the liver with splenomegaly, SLE, Gaucher's disease.
5. Cachexia and debility
6. Anaphylactoid shock
7. Certain rare hereditary, congenital or familial disorders, e.g. cyclic neutropenia.

Defective Functions

1. Defective chemotaxis, e.g. in lazy-leukocyte syndrome; following corticosteroid therapy, aspirin ingestion, alcoholism, and in myeloid leukemia.
2. Defective phagocytosis, e.g. in hypogammaglobulinemia, hypocomplementemia, after splenectomy, in sickle cell disease.

3. Defective killing, e.g. in chronic granulomatous disease, Chédiak-Higashi syndrome, myeloid leukemias.

Q. 6. Write a short note on thrombocytopenia.

(TNMGR, Oct. 1999)

Ans. Thrombocytopenia is defined as a reduction in the peripheral blood platelet count below the lower limit of normal, i.e. below 150,000/ μ l. Thrombocytopenia may result from 4 main groups of causes:

1. Impaired platelet production.
2. Accelerated platelet destruction.
3. Splenic sequestration.
4. Dilutional loss.

The common and important causes

1. **Drug-induced thrombocytopenia:** Chemotherapeutic agents, antibiotics (sulfonamides, PAS, rifampicin, penicillins), drugs used in cardiovascular diseases (digitoxin, thiazide diuretics), diclofenac, acyclovir, heparin and excessive consumption of ethanol. Clinically, the patient presents with acute purpura. The platelet count is markedly lowered, often below 10,000/ μ l and the bone marrow shows normal or increased number of megakaryocyte.

The immediate treatment is to stop or replace the suspected drug with instruction to the patient to avoid taking the offending drug in future. Occasional patients may require temporary support with glucocorticoids, plasmapheresis or platelet transfusions.

2. **Immune thrombocytopenic purpura (ITP):** Characterized by immunologic destruction of platelets and normal or increased megakaryocyte in the bone marrow.

Pathogenesis

Acute ITP: This is a self-limited disorder, seen most frequently in children following recovery from a viral illness. The mechanism of acute ITP is by formation of immune complexes containing viral antigens, and by formation of antibodies against viral antigens which cross react with platelets and lead to their immunologic destruction.

Chronic ITP: Chronic ITP occurs more commonly in adults, particularly in women of child-bearing age (20–40 years). Pathogenesis of chronic ITP is explained by formation of anti-platelet autoantibodies. These antibodies are directed against target antigens on the platelet glycoproteins.

The usual manifestations are petechial hemorrhages, easy bruising, and mucosal bleeding such as menorrhagia in women, nasal bleeding, bleeding from gums,

melen and hematuria. Intracranial hemorrhage is, however, rare. Splenomegaly and hepatomegaly may occur in cases with chronic ITP but lymphadenopathy is quite uncommon in either type of ITP.

Laboratory Findings

1. Platelet count is markedly reduced
2. Blood film—occasional platelets
3. Bone marrow—increased number of megakaryocyte.

Treatment

1. Corticosteroid therapy
2. Immunosuppressive drugs
3. Splenectomy
4. Platelet transfusions

Thrombotic thrombocytopenic purpura (TTP): Triad of thrombocytopenia, microangiopathic hemolytic anemia and formation of microthrombi.

Pathogenesis

TTP is initiated by endothelial injury followed by release of von Willebrand factor and other procoagulant material from endothelial cells, leading to the formation of microthrombi.

Laboratory Findings

1. Thrombocytopenia
2. Microangiopathic hemolytic anemia with negative Coombs' test.
3. Leukocytosis, sometimes with leukemoid reaction
4. Bone marrow examination reveals normal or slightly increased megakaryocyte.
5. Diagnosis is established by examination of biopsy (e.g. from gingiva).

Q. 7. Write a short note on transfusion reactions.

(TNMGR, March 2002; KLE Uni. Jan. 2009)

Ans. Transfusion reactions are generally classified into 2 types:

I. Immunologic transfusion reactions may be against red blood cells (hemolytic reactions), leukocytes, platelets or immunoglobulins. These are as under.

1. Hemolytic transfusion reactions

- a. **Intravascular hemolysis:** Due to ABO incompatibility. The symptoms include restlessness, anxiety, flushing, chest or lumbar pain, tachypnea, tachycardia and nausea, followed by shock and renal failure.
- b. **Extravascular hemolysis:** Due to immune antibodies of the Rh system, malaise and fever but shock and renal failure may rarely occur. Some patients develop delayed reactions because of previous

transfusion or pregnancy, in which the patient develops anemia due to destruction of red cells in the RE system about a week after transfusion (**anamnestic reaction**).

2. **Transfusion-related acute lung injury (TRALI):** This is an uncommon reaction resulting from transfusion of donor plasma containing high levels of anti-HLA antibodies which bind to leukocytes of recipient.
3. **Other allergic reactions**
 - i. **Febrile reaction:** Immunologic reaction against white blood cells, platelets, or IgA class immunoglobulins.
 - ii. Anaphylactic shock.
 - iii. Allergic reactions: Urticaria.
 - iv. Transfusion-related graft-versus-host disease.

II. Non-immune transfusion reactions

1. Circulatory overload
2. Massive transfusion
3. Transmission of infection
4. Air embolism
5. Thrombophlebitis
6. Transfusion hemosiderosis.

Q. 8. Describe the diseases of red blood cells.

(MUHS, May 2012; HP, May 2012)

Ans.

1. **Polycythemia:** Abnormal increase in RBC count:
 - a. **Primary (polycythemia vera):** In myeloproliferative disorders.
 - b. **Secondary polycythemia:** Secondary to pathological conditions. For example, congenital heart disease.
2. **Anemia:** Abnormal decrease in RBC count.
3. **Microcyte:** Smaller RBC. For example, iron deficiency anemia.
4. **Macrocyte:** Abnormally large RBC. For example, megaloblastic anemia.
5. **Crenation:** Shrinkage as in hypertonic conditions.
6. **Spherocytosis:** Globular form as in hypotonic conditions.
7. **Elliptocytosis:** Elliptical shape as in certain types of anemia.
8. **Sickle cell:** Crescentic shape as in sickle cell anemia.
9. **Poikilocytosis:** Unusual shapes due to deformed cell membrane. The shape will be of flask, hammer or any other unusual shape.
10. **Punctate basophilism:** Striated appearance of RBCs by the presence of dots of basophilic materials (porphyrin) is called punctate basophilism. It occurs in conditions like lead poisoning.

11. **Ring in red blood cells:** Ring or twisted strands of basophilic material appear in the periphery of the RBCs. This is also called the goblet ring. This appears in the RBCs in certain types of anemia.

12. **Howell-Jolly bodies:** In certain types of anemia, some nuclear fragments are present in the ectoplasm of the RBCs. These nuclear fragments are called Howell-Jolly bodies.

Q. 9. Write a short note on hemophilia.

(MUHS, May 2015)

Ans. **Classic hemophilia (hemophilia A):** Second most common hereditary coagulation disorder next to von Willebrand's disease. The disorder is inherited as a sex-(X-) linked recessive trait and, therefore, manifests clinically in males, while females are usually the carriers.

Pathogenesis

Hemophilia A is caused by quantitative reduction of factor VIII in 90% of cases, while 10% cases have normal or increased level of factor VIII with reduced activity.

Clinical Features

Haemophilics bleeding can involve any organ but occurs most commonly as recurrent painful hemarthroses and muscle hematomas, and sometimes as hematuria. Spontaneous intracranial hemorrhage and oropharyngeal bleeding.

Laboratory Findings

1. Whole blood coagulation time—prolonged
2. Prothrombin time—normal
3. Activated partial thromboplastin time (APTT or PTTK)—typically prolonged.
4. Specific assay for factor VIII—lowered.

Treatment

Symptomatic patients with bleeding episodes are treated with factor VIII replacement therapy, consisting of factor VIII concentrates or plasma cryoprecipitate.

Christmas Disease (Hemophilia B)

Inherited deficiency of factor IX (Christmas factor or plasma thromboplastin component) produces Christmas disease or hemophilia B. Hemophilia B is rarer than hemophilia A. The inheritance pattern and clinical features of factor IX deficiency are indistinguishable from those of classic hemophilia but accurate laboratory diagnosis is critical since hemophilia B requires treatment with different plasma fraction. The usual screening tests for coagulation are similar to those in classic hemophilia but bioassay of factor IX reveals lowered activity.

Treatment

Therapy in symptomatic hemophilia B consists of infusion of either fresh frozen plasma or plasma enriched with factor IX.

Q. 10. Write a short note on bleeding time and clotting time. (TNMGR, April 1998)

Ans. Bleeding time (BT) is the time interval from oozing of blood after a cut or injury till arrest of bleeding. Usually, it is determined by Duke method using blotting paper or filter paper method. Its normal duration is 3 to 6 minutes. It is prolonged in purpura.

Clotting time (CT) is the time interval from oozing of blood after a cut or injury till the formation of clot. It is usually determined by capillary tube method. Its normal duration is 3 to 8 minutes. It is prolonged in hemophilia.

Q. 11. Define hemorrhage. Classify it. Describe the management of secondary hemorrhage from extraction socket. (BFUHS, Oct. 2010)

Ans. Hemorrhage is the escape of blood from a blood vessel.

Classification

a. Based on the type of blood vessel involved

1. *Arterial hemorrhage*: Bleeding from ruptured artery. It is pulsatile, brisk and bright red in color
2. *Venous hemorrhage*: Bleeding from veins. Non-pulsatile, dark in color.

3. *Capillary hemorrhage*: Oozing from the capillaries. The blood is bluish red in color.

b. Based on the duration

1. *Primary hemorrhage*: The bleeding at the time of injury.
2. *Secondary hemorrhage*: The bleeding after 24 hours to several days.
3. *Intermediate hemorrhage*: The bleeding occurring within eight hours after stoppage of primary bleeding.

Management of Secondary Bleeding

Causes

- a. Dislodgement of clot
- b. Secondary trauma to wound
- c. Infection
- d. Elevation of blood pressure

Management

a. Local hemostatic measures

1. *Mechanical methods*: Local pressure, use of hemostat, suture and ligation, embolization of the vessels.
2. *Thermal agents*: Cautery, electrosurgery, cryosurgery, argon-beam coagulator.
3. *Chemical methods*: Astringents and styptics (tannic acid, silver nitrate), bone wax, thrombin, gelform, oxycel, surgical, fibrin glue, adrenaline, whole blood, platelet-rich plasma, fresh frozen plasma, cryoprecipitate.

Pharmacology

1. PHARMACODYNAMIC AND PHARMACOKINETIC OF DRUGS

Q. 1. Describe various routes of drug administration.

(MAHE, July 2001; RGUHS, September 2007; TNMGR, March 2009, 2010)

Ans. Factors governing choice of route

1. Physical and chemical properties of the drug—solid/liquid/gas; solubility, stability, pH, irritancy.
2. Site of desired action—localized and approachable or generalized and not approachable.
3. Rate and extent of absorption of the drug from different routes.
4. Effect of digestive juices and first pass metabolism on the drug.
5. Rapidity with which the response is desired—routine treatment or emergency.
6. Accuracy of dosage required—IV and inhalational can provide fine tuning.
7. Condition of the patient.

A. Local Routes

1. **Topical:** External application of the drug to the surface for localized action. It is often more convenient as well as encouraging to the patient. Drugs can be efficiently delivered to the localized lesions on skin, oropharyngeal/nasal mucosa, eyes, ear canal, anal canal or vagina in the form of lotion, ointment, cream, powder, rinse, paints, drops, spray, lozenges, suppositories or pessaries.
2. **Deeper tissues:** Certain deep areas can be approached by using a syringe and needle, but the drug should be such that systemic absorption is slow, e.g. intra-articular injection, infiltration around a nerve or intrathecal injection, retrobulbar injection.
3. **Arterial supply:** Close intra-arterial injection is used for contrast media in angiography; anticancer drugs

can be infused in femoral or brachial artery to localize the effect for limb malignancies.

B. Systemic Routes

1. **Oral:** It is safer, more convenient, does not need assistance, non-invasive, often painless, the medicament need not be sterile and so is cheaper. Both solid dosage forms (powders, tablets, capsules, spansules, gastrointestinal therapeutic systems—GITs) and liquid dosage forms (elixirs, syrups, emulsions, mixtures) can be given orally.

Limitations

- Action of drugs is slower and thus not suitable for emergencies.
 - Unpalatable drugs are difficult to administer.
 - May cause nausea and vomiting.
 - Cannot be used for uncooperative/unconscious/vomiting patient.
 - Absorption of drugs may be variable and erratic.
 - Drugs may be destroyed by digestive juices.
2. **Sublingual or buccal:** The tablet or pellet containing the drug is placed under the tongue or crushed in the mouth and spread over the buccal mucosa. Absorption is relatively rapid—action can be produced in minutes. The chief advantage is that liver is bypassed and drugs with high first pass metabolism can be absorbed directly into systemic circulation. Drugs given sublingually are: Glycero trinitrate (GTN), buprenorphine.
 3. **Rectal:** Certain irritant and unpleasant drugs can be put into rectum as suppositories or retention enema for systemic effect. This route can also be used when the patient is having recurrent vomiting or is unconscious. However, absorption is slower, irregular and often unpredictable.
 4. **Cutaneous:** Highly lipid soluble drugs can be applied over the skin for slow and prolonged absorption. The

liver is also bypassed. Absorption of the drug can be enhanced by rubbing the preparation, by using an oily base and by an occlusive dressing. **Transdermal therapeutic systems** are devices in the form of adhesive patches of various shapes and sizes (5–20 cm²) which deliver the contained drug at a constant rate into systemic circulation. The drug is held in a reservoir between an occlusive backing film and a rate controlling micropore membrane, the under surface of which is smeared with an adhesive impregnated with priming dose of the drug. The adhesive layer is protected by another film that is to be peeled off just before application. The drug is delivered at the skin surface by diffusion for percutaneous absorption into circulation.

5. **Inhalation:** Volatile liquids and gases are given by inhalation for systemic action, e.g. general anesthetics. Action is very rapid.
6. **Nasal:** The mucous membrane of the nose can readily absorb many drugs; digestive juices and liver are bypassed.
7. **Parenteral** (Par: beyond, enteral: intestinal). It refers to administration by injection which takes the drug directly into the tissue fluid or blood without having to cross the intestinal mucosa.

Advantages

1. Drug action is faster and for sure.
2. Gastric irritation and vomiting are not provoked.
3. Can be used in unconscious, uncooperative or vomiting patients.
4. No chances of interference by food or digestive juices.
5. No first pass metabolism.

Disadvantages

1. Only sterilized preparation can be used.
2. Expensive.
3. Invasive and painful.
4. Assistance required.
5. Chances of local tissue injury.
6. More risky than oral route.

Various parenteral routes are

- i. **Subcutaneous:** The drug is deposited in the loose subcutaneous tissue which is richly supplied by nerves but is less vascular. Only small volumes can be injected. Self-injection is possible. Some special forms of this route are:
 - a. **Dermojet:** A high velocity jet of drug solution is projected from a microfine orifice using a gun-like implement. It is essentially painless and suited for mass inoculations.

- b. **Pellet implantation:** The drug in the form of a solid pellet is introduced with a trochar and cannula. For example, DOCA, testosterone.

- c. **Sialistic (nonbiodegradable) and biodegradable implants:** Crystalline drug is packed in tubes or capsules made of suitable materials and implanted under the skin. This has been tried for hormones and contraceptives (e.g. Norplant).

- ii. **Intramuscular:** The drug is injected in one of the large skeletal muscles—deltoid, triceps, gluteus maximus, rectus femoris, etc. Muscle is less richly supplied with sensory nerves and is more vascular (absorption of drugs is faster). It is less painful, but self-injection is often impracticable. Intramuscular injections should be avoided in anticoagulant treated patients.

- iii. **Intravenous:** The drug is injected as a bolus (Greek: bolos—lump) or infused slowly over hours in one of the superficial veins. The drug reaches directly into the bloodstream and effects are produced immediately. The hazards are—thrombophlebitis and necrosis of adjoining tissues if extravasation occurs. The dose of the drug required is smallest (bioavailability is 100%) and even large volumes can be infused. One big advantage with this route is response is accurately measurable (e.g. BP) and the titration of the dose with the response is possible. However, this is the most risky route—vital organs like heart; brain, etc. get exposed to high concentrations of the drug.

- iv. **Intradermal injection:** The drug is injected into the skin raising a bleb (e.g. BCG vaccine, sensitivity testing) or scarring/multiple puncture of the epidermis through a drop of the drug is done.

Q. 2. Write a short note on saturation kinetics.

(TNMGR, April 1998)

Ans. Pharmacokinetics is the quantitative study of drug movement in, through and out of the body. It involves absorption, distribution, metabolism and excretion.

1. **Absorption:** Absorption is movement of the drug from its site of administration into the circulation. Not only the fraction of the administered dose that gets absorbed but also the rate of absorption is important. Except when given IV, the drug has to cross biological membranes.

2. **Distribution:** Once a drug has gained access to the bloodstream, it gets distributed to other tissues that initially had no drug, concentration gradient being in the direction of plasma to tissues. The extent of distribution of a drug depends on its lipid solubility, ionization at physiological pH (a function of its pKa),

extent of binding to plasma and tissue proteins, presence of tissue-specific transporters and differences in regional blood flow. Movement of drug proceeds until an equilibrium is established between unbound drug in plasma and tissue fluids. Subsequently, there is a parallel decline in both due to elimination.

3. Biotransformation (metabolism): Biotransformation means chemical alteration of the drug in the body. It is needed to render non-polar (lipid-soluble) compounds polar (lipid insoluble) so that they are not reabsorbed in the renal tubules and are excreted. Most hydrophilic drugs, e.g. streptomycin, neostigmine, pancuronium, etc. are a little biotransformed and are largely excreted unchanged. Mechanisms which metabolize drugs have developed to protect the body from ingested toxins. The primary site for drug metabolism is liver; others are—kidney, intestine, lungs and plasma. Biotransformation of drugs may lead to the following:

- i. *Inactivation:* Most drugs and their active metabolites are rendered inactive or less active, e.g. ibuprofen, paracetamol, lidocaine, chloramphenicol, propranolol and its active metabolite 4-hydroxypropranolol.
- ii. *Active metabolite from an active drug:* Many drugs have been found to be partially converted to one or more active metabolite; the effects observed are the sum total of that due to the parent drug and its active metabolite(s).
- iii. *Activation of inactive drug:* A few drugs are inactive as such and need conversion in the body to one or more active metabolites. Such a drug is called a prodrug. The prodrug may offer advantages over the active form in being more stable, having better bioavailability or other desirable pharmacokinetic properties or less side effects and toxicity. Some prodrugs are activated selectively at the site of action.

Biotransformation reactions can be classified into:

- a. **Nonsynthetic/phase I/functionalization reactions:** A functional group is generated or exposed, metabolite may be active or inactive.
 - b. **Synthetic/conjugation/phase II reactions:** Metabolite is mostly inactive; except a few drugs, e.g. glucuronide conjugate of morphine and sulfate conjugate of minoxidil are active.
- 4. Excretion:** Excretion is the passage out of systemically absorbed drug. Drugs and their metabolites are excreted in:
1. Urine
 2. Feces

3. Exhaled air
4. Saliva and sweat
5. Milk

Kinetics of elimination: The knowledge of kinetics of elimination of a drug provides the basis for, as well as serves to devise rational dosage regimens and to modify them according to individual needs. There are three fundamental pharmacokinetic parameters, viz. bioavailability (F), volume of distribution (V) and clearance (CL) which must be understood. Drug is eliminated only from the central compartment (blood) which is in equilibrium with peripheral compartments including the site of action.

Clearance (CL): The clearance of a drug is the theoretical volume of plasma from which the drug is completely removed in unit time (analogy creatinine clearance). It can be calculated as

CL = Rate of elimination/C ; where C is the plasma concentration.

For majority of drugs the processes involved in elimination are not saturated over the clinically obtained concentrations, they follow:

First order (exponential) kinetics: The rate of elimination is directly proportional to the drug concentration, CL remains constant; or a constant fraction of the drug present in the body is eliminated in unit time.

Zero order (linear) kinetics: The rate of elimination remains constant irrespective of drug concentration, CL decreases with increase in concentration; or a constant amount of the drug is eliminated in unit time, e.g. ethyl alcohol. The elimination of some drugs approaches saturation over the therapeutic range, kinetics changes from first order to zero order at higher doses. As a result plasma concentration increases disproportionately with increase in dose, as occurs in case of phenytoin, tolbutamide, theophylline, and warfarin.

Plasma half-life: The plasma half-life ($t_{1/2}$) of a drug is the time taken for its plasma concentration to be reduced to half of its original value.

As such, half-life is a derived parameter from two variables V and CL both of which may change independently, i.e. after

1. $t_{1/2}$: 50% drug is eliminated.
2. $t_{1/2}$: 75% (50 + 25) drug is eliminated.
3. $t_{1/2}$: 87.5% (50 + 25 + 12.5) drug is eliminated.
4. $t_{1/2}$: 93.75% (50 + 25 + 12.5 + 6.25) drug is eliminated.

Thus, nearly complete drug elimination occurs in 4–5 half lives.

For drugs eliminated by: First order kinetics— $t_{1/2}$ remains constant because V and CL do not change with dose.

Zero order kinetics— $t_{1/2}$ increases with dose because CL progressively decreases as dose is increased.

Half-life of some representative drugs

Aspirin 4 hr; digoxin 40 hr; penicillin-G 30 min; digitoxin 7 days; doxycycline 20 hr; phenobarbitone 90 hr.

Plateau principle: When constant dose of a drug is repeated before the expiry of 4 $t_{1/2}$, it would achieve higher peak concentration, because some remnant of the previous dose will be present in the body. This continues with every dose until progressively increasing rate of elimination balances the amount administered over the dose interval. Subsequently plasma concentration plateaus and fluctuates about an average steady-state level. This is known as the **plateau principle** of drug accumulation. Steady-state is reached in 4–5 half lives unless dose interval is very much longer than $t_{1/2}$. The amplitude of fluctuations in plasma concentration at steady-state depends on the dose interval relative to the $t_{1/2}$, i.e. the difference between the maximum and minimum levels is less if smaller doses are repeated more frequently (dose rate remaining constant).

Q. 3. Write about mechanism of action of drug.

(TNMGR, March 2008)

Ans. Pharmacodynamic is the study of drug effects. Modification of the action of one drug by another drug is also an aspect of pharmacodynamic.

Principles of drug action: The basic types of drug action can be broadly classed as:

- 1. Stimulation:** It refers to selective enhancement of the level of activity of specialized cells, e.g. adrenaline stimulates heart.
- 2. Depression:** It means selective diminution of activity of specialized cells, e.g. barbiturates depress CNS.
- 3. Irritation:** This connotes a nonselective, often noxious effect and is particularly applied to less specialized cells (epithelium, connective tissue). Mild irritation may stimulate associated function, e.g. bitters increase salivary and gastric secretion. But strong irritation results in inflammation, corrosion, necrosis and morphological damage.
- 4. Replacement:** This refers to the use of natural metabolites, hormones or their congeners in deficiency states, e.g. levodopa in parkinsonism, insulin in diabetes mellitus, iron in anemia.
- 5. Cytotoxic action:** Selective cytotoxic action for invading parasites or cancer cells, attenuating them without significantly affecting the host cells is

utilized for cure/palliation of infections and neoplasms, e.g. penicillin, chloroquine, zidovudine, cyclophosphamide, etc.

Mechanism of drug action: Only a few drugs act by virtue of their simple physical or chemical property; examples are:

- Bulk laxatives (ispaghula)—physical mass.
- Antacids—neutralization of gastric HCl.
- Pot. Permanganate—oxidizing property.
- Chelating agents (EDTA, dimercaprol)—chelation of heavy metals.

Most drugs produce their effects by binding to protein molecules. Four primary drug targets are

I. Enzymes: Drugs can either increase or decrease the rate of enzymatically mediated reactions, e.g. pyridoxine acts as a cofactor and increases decarboxylase activity. Several enzymes are stimulated through receptors and second messengers, e.g. adrenaline stimulates hepatic glycogen phosphorylase through β receptors and cyclic AMP. Apparent increase in enzyme activity can also occur by enzyme induction. Inhibition of enzymes is a common mode of drug action.

a. **Nonspecific inhibition:** Many chemicals alter the tertiary structure of any enzyme with which they come in contact and thus inhibit it. Heavy metal salts, strong acids and alkalis, alcohol, formaldehyde, phenol inhibit enzymes nonspecifically.

b. **Specific inhibition:** Many drugs inhibit a particular enzyme without affecting others. Such inhibition is either competitive or noncompetitive.

i. **Competitive (equilibrium type):** The drug being structurally similar competes with the normal substrate for the catalytic binding site of the enzyme so that the product is not formed or a nonfunctional product is formed.

- Physostigmine and neostigmine compete with acetylcholine for cholinesterase.
- Sulfonamides compete with PABA for bacterial folate synthetase.

A nonequilibrium type of enzyme inhibition can also occur with drugs which react with the same catalytic site of the enzyme but either form strong covalent bonds or have such high affinity for the enzyme that the normal substrate is not able to displace the inhibitor, e.g. organophosphates react covalently with the esteratic site of the enzyme cholinesterase.

ii. **Noncompetitive:** The inhibitor reacts with an adjacent site and not with the catalytic site, but alters the enzyme in such a way that it loses its catalytic property.

II. Ion channels: Proteins which act as ion selective channels participate in transmembrane signaling and regulate intracellular ionic composition. This makes them a common target of drug action. Drugs can affect ion channels either through specific receptors (ligand gated ion channels, G-protein operated ion channels), or by directly binding to the channel and affecting ion movement through it, e.g. local anesthetics which physically obstruct voltage sensitive Na^+ channels.

III. Transporters: Several substrates are translocated across membranes by binding to specific transporters (carriers) which either facilitate diffusion in the direction of the concentration gradient or pump the metabolite/ion against the concentration gradient using metabolic energy. Many drugs produce their action by directly interacting with the solute carrier class of transporter proteins to inhibit the ongoing physiological transport of the metabolite/ion. Examples are:

- Desipramine and cocaine block neuronal reuptake of noradrenaline (NA) by interacting with norepinephrine transporter (NET).
- Amphetamines selectively block dopamine reuptake in brain neurons by dopamine transporter (DAT).

IV. Receptors: The largest number of drugs acts through specific 'receptors'.

1. G-protein coupled receptors (GPCR): These are a large family of cell membrane receptors which are linked to the effector (enzyme/channel/carrier protein) through one or more GTP-activated proteins (G-proteins) for response effectuation. The agonist binding site is located between the helices on the extracellular face, while another recognition site formed by cytosolic segments binds the coupling G-protein. In the inactive state GDP is bound to their exposed domain; activation through the receptor leads to displacement of GDP by GTP.

Gs : Adenylyl cyclase \uparrow , Ca^{2+} channel \uparrow

Gi : Adenylyl cyclase \downarrow , K^+ channel \uparrow

Go : Ca^{2+} channel \downarrow

Gq : Phospholipase C \uparrow

G13 : Na^+/H^+ exchange \uparrow

One receptor can utilize more than one G-protein (agonist pleiotropy). There are three major effector pathways through which GPCRs function.

a. Adenylyl cyclase: cAMP pathway activation of AC results in intracellular accumulation of second messenger cAMP which functions mainly through cAMP-dependent protein kinase (PKA). The PKA phosphorylates and alters the function of many enzymes, ion channels, transporters and structural proteins.

b. Phospholipase C: IP3-DAG pathway: Activation of phospholipase C (PLC) hydrolyses the membrane phospholipid phosphatidyl inositol 4, 5-bisphosphate (PIP2) to generate the second messengers inositol 1,4,5-trisphosphate (IP3) and diacylglycerol (DAG). The IP3 mobilizes Ca^{2+} from intracellular organellar depots and DAG enhances protein kinase C (PKC) activation by Ca^{2+} .

c. Channel regulation: The activated G-proteins can also open or close ionic channels specific for Ca^{2+} , K^+ or Na^+ , without the intervention of any second messenger like cAMP or IP3, and bring about hyperpolarization/depolarization/changes in intracellular Ca^{2+} .

2. Receptors with intrinsic ion channel: These cell surface receptors, also called ligand gated ion channels, enclose ion selective channels (for Na^+ , K^+ , Ca^{2+} or Cl^-) within their molecules. Agonist binding opens the channel and causes depolarization/hyperpolarization/changes in cytosolic ionic composition, depending on the ion that flows through.

3. Enzyme-linked receptors: This class of receptors has a subunit with enzymatic property or binds a JAK (Janus-Kinase) enzyme on activation. The agonist binding site and the catalytic site lie respectively on the outer and inner face of the plasma membrane.

4. Receptors regulating gene expression (transcription factors): These are intracellular (cytoplasmic or nuclear) soluble proteins which respond to lipid soluble chemical messengers that penetrate the cell. The receptor protein is inherently capable of binding to specific genes, but is kept inhibited till the hormone binds near its carboxy terminus and exposes the DNA binding regulatory segment located in the middle of the molecule. All steroidal hormones, thyroxine, vit D and vit A function in this manner.

Functions of receptors

- To propagate regulatory signals from outside to within the effector cell when the molecular species carrying the signal cannot itself penetrate the cell membrane.
- To amplify the signal.
- To integrate various extracellular and intracellular regulatory signals.
- To adapt to short-term and long-term changes in the regulatory milieu and maintain homeostasis.

Nonreceptor-mediated drug action: This refers to drugs which do not act by binding to specific regulatory

macromolecules. Drug action by purely physical or chemical means, interactions with small molecules or ions as well as direct interaction with enzymes, ionic channels and transporters has already been described. In addition, there are drugs like alkylating agents which react covalently with several critical biomolecules, especially nucleic acids, and have cytotoxic property useful in the treatment of cancer.

Q. 6. Discuss the role of receptors in the mechanism of drug action. (TNMGR, Oct. 2012)

Ans. Receptor is defined as a macromolecule or binding site located on the surface or inside the effector cell that serves to recognize the signal molecule/drug and initiate the response to it, but itself has no other function.

Drug action through receptors

1. *Receptor occupation theory*: This theory states that the drug action is based on occupation of receptors by specific drugs and that the pace of a cellular function can be altered by interaction of these receptors with drugs.
2. *The two-state receptor model*: The receptor is believed to exist in two interchangeable states: R_a (active) and R_i (inactive) which are in equilibrium. In the case of majority of receptors, the R_i state is favored at equilibrium—no/very weak signal is generated in the absence of the agonist—the receptor exhibits no constitutive activation. The agonist (A) binds preferentially to the R_a conformation and shifts the equilibrium $\rightarrow R_a$ predominates and a response is generated depending on the concentration of A.

Nature of receptors

1. *Physiological receptors*: Mediate responses to transmitters, hormones, autacoids and other endogenous signal molecules. For example, cholinergic, adrenergic, histaminergic, steroid, leukotriene, insulin.
2. *Drug receptors*: No known physiological ligands. For example, benzodiazepine receptor, sulfonylurea receptor.

Receptor subtypes: The following criteria have been utilized in classifying receptors:

- a. *Pharmacological criteria*: Classification is based on relative potencies of selective agonists and antagonists. This was used in delineating M and N cholinergic, α and β adrenergic receptors, etc.
- b. *Tissue distribution*: The relative organ/tissue distribution is the basis for designating the subtype.
- c. *Ligand binding*: Measurement of specific binding of high affinity radio-labeled ligand to cellular fragments *in vitro*, and its displacement by various selective

agonists/antagonists is used to delineate receptor subtypes. For example, subtypes of 5-HT receptors.

- d. *Transducer pathway*: Receptor subtypes may be distinguished by the mechanism through which their activation is linked to the response, e.g. M cholinergic receptor acts through G-proteins, while N cholinergic receptor gates influx of Na^+ ions.
- e. *Molecular cloning*: The receptor protein is cloned and its detailed amino acid sequence as well as three-dimensional structure is worked out. Subtypes are designated on the basis of sequence homology.
- f. *Silent receptors*: These are sites which bind specific drugs but no pharmacological response is elicited. They are better called drug acceptors or sites of loss, e.g. plasma proteins which have binding sites for many drugs.

Q. 4. Write about local drug delivery systems in the oral cavity. (TNMGR, March 2007; RGUHS, April 2007)

Ans. These include:

- a. *Oral rinses*: These require patient compliance; easy to use, high concentration of the agent can be delivered.
- b. *Oral irrigation*: Easy to use, high concentration of the agent can be delivered; subgingival areas can be irrigated safely.
- c. *Controlled release device*: It is reproducible and drug can be delivered at constant rate. It requires less frequent administration and has greater patient compliance, with reduced side effects.

Types

1. *Reservoirs without rate controlling system*: Hollow fibers filled with agent.
2. *Reservoirs with rate controlling system*: Microcapsules filled with agent.
3. *Monolithic system*: Agent dispersed in inert polymeric matrix.
4. *Laminated system*: Multiple layers of polymers with different diffusion capacity.

Q. 5. Write a short note on drug antagonism.

(TNMGR, March 2007)

Ans. When one drug decreases or abolishes the action of another, they are said to be antagonistic. Effect of drug A + B < effect of drug A + effect of drug B.

Types: Based on mechanism of antagonism

1. *Physical antagonism*: Based on the physical property of the drugs, e.g. charcoal adsorbs alkaloid—used in alkaloid poisoning.
2. *Chemical antagonism*: Drug reacts chemically and form inactive product. For example,

$$KMnO_4 + \text{Alkaloids} \rightarrow \text{Inactive product.}$$

3. **Physiological/functional antagonism:** The two drugs act on different receptors or by different mechanism, but have opposite effect on the same physiological function.

For example,

Glucagon + Insulin → Effects of blood sugar level.

4. **Receptor antagonism:** One drug (antagonist) blocks the receptor action of the other (agonist).

Receptor antagonism can be competitive or non-competitive

a. Competitive antagonism

- i. **Equilibrium type:** The antagonist is chemically similar to the agonist, competes with it and binds to the same site to the exclusion of the agonist molecules. Because the antagonist has affinity but no intrinsic activity, no response is produced. Antagonist binding is reversible and depends on the relative concentration of the agonist and antagonist molecules, higher concentration of the agonist progressively overcomes the block.

- ii. **Nonequilibrium (competitive) antagonism:** Certain antagonists bind to the receptor with strong (covalent) bonds or dissociate from it slowly so that agonist molecules are unable to reduce receptor occupancy of the antagonist molecules. An irreversible or nonequilibrium antagonism is produced.

- b. **Non-competitive:** The antagonist is chemically unrelated to the agonist, binds to a different allosteric site altering the receptor in such a way that it is unable to combine with the agonist, or unable to transduce the response.

Q. 7. Write in detail about adverse drug reactions.

(TNMGR, April 1995)

Q. Write a short note on drug allergy.

(TNMGR, Oct. 2013)

Ans. It is defined as "any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug."

A. According to Predictability of Adverse Effects

1. **Predictable (type A or augmented) reactions:** These are based on the pharmacological properties of the drug, include side effects, toxic effects and consequences of drug withdrawal. They are more common, dose related and mostly preventable and reversible.
2. **Unpredictable (type B or bizarre) reactions:** These are based on peculiarities of the patient and not on

drug's known actions; include allergy and idiosyncrasy. They are less common, often non-dose related, generally more serious and require withdrawal of the drug.

B. According to Severity of Adverse Effects

1. **Minor:** No therapy, antidote or prolongation of hospitalization is required.
2. **Moderate:** Requires change in drug therapy, specific treatment or prolongs hospital stay.
3. **Severe:** Potentially life-threatening, causes permanent damage or requires intensive medical treatment.
4. **Lethal:** Directly or indirectly contributes to death of the patient.

C. Adverse Drug Effects may be Categorized into

1. **Side effects:** These are unwanted but often unavoidable pharmacodynamic effects that occur at therapeutic doses. Reduction in dose generally ameliorates the symptoms. For example, atropine causes dryness of mouth. Codeine used for cough produces constipation.
2. **Secondary effects:** These are indirect consequences of a primary action of the drug. For example, suppression of bacterial flora by tetracyclines leading to super infections.
3. **Toxic effects:** These are the result of excessive pharmacological action of the drug due to over dosage or prolonged use. For example, coma by barbiturates, complete AV block by digoxin, bleeding due to heparin.
4. **Intolerance:** It is the appearance of characteristic toxic effects of a drug in an individual at therapeutic doses. It indicates a low threshold of the individual to the action of a drug. For example, a single dose of trifluoromazine induces muscular dystonias in some individuals.
5. **Idiosyncrasy:** It is genetically determined abnormal reactivity to a chemical. The drug interacts with some unique feature of the individual, and produces the uncharacteristic reaction. For example, barbiturates cause excitement and mental confusion in some individuals.
6. **Drug allergy:** It is an immunologically mediated reaction producing stereotype symptoms which are unrelated to the pharmacodynamic profile of the drug, generally occur even with much smaller doses and have a different time course of onset and duration. This is also called drug hypersensitivity; but does not refer to increased response which is called super sensitivity. Prior sensitization is needed

and a latent period of at least 1–2 weeks is required after the first exposure. The drug or its metabolite acts as antigen (AG) or more commonly hapten (incomplete antigen and induce production of antibody (AB)/sensitized lymphocytes.

Mechanism and types of allergic reactions

a. Humoral

Type I (anaphylactic) reactions: Reaginic antibodies (IgE) are produced which get fixed to the mast cells. On exposure to the drug, AG:AB reaction takes place on the mast cell surface releasing mediators like histamine, 5-HT, leukotrienes especially LT-C4 and D4, prostaglandins, etc. resulting in urticaria, itching, angioedema, bronchospasm, rhinitis or anaphylactic shock.

Type II (cytolytic) reactions: Drug and component of a specific tissue cell act as AG. The resulting antibodies (IgG, IgM) bind to the target cells; on re-exposure AG:AB reaction takes place on the surface of these cells, complement is activated and cytolysis occurs, e.g. thrombocytopenia, agranulocytosis, aplastic anemia, hemolysis, organ damage, and systemic lupus erythematosus.

Type III (retarded, arthus) reactions: These are mediated by circulating antibodies (predominantly IgG). AG:AB complexes bind complement and precipitate on vascular endothelium giving rise to a destructive inflammatory response. Manifestations are rashes, serum sickness (fever, arthralgia, and lymphadenopathy), and polyarteritis nodosa, Stevens-Johnson syndrome. The reaction usually subsides in 1–2 weeks.

b. Cell mediated

Type IV (delayed hypersensitivity) reactions: These are mediated through production of sensitized T-lymphocytes carrying receptors for the AG. On contact with the AG, these T cells produce lymphokines which attract granulocytes and generate an inflammatory response, e.g. contact dermatitis, some rashes, fever, photosensitization. The reaction generally takes >12 hours to develop.

7. Photosensitivity: It is a cutaneous reaction resulting from drug-induced sensitization of the skin to UV radiation. The reactions are of two types:

- a. **Phototoxic:** Drug or its metabolite accumulates in the skin, absorbs light and undergoes a photochemical reaction followed by a photo-biological reaction resulting in local tissue damage (sunburn-like), i.e. erythema, edema, blistering followed by hyper-pigmentation and desquamation. The shorter wave lengths (290–320 nm, UVB) are responsible.

- i. **Acute phototoxic reactions:** Tetracyclines (especially demeclocycline) and tar products.
- ii. **Chronic phototoxic reactions:** Nalidixic acid, fluoroquinolones, sulfones, sulfonamides, phenothiazines, thiazides, amiodarone.

This type of reaction is more common than photo-allergic reaction.

- b. **Photoallergic:** Drug or its metabolite induces a cell-mediated immune response which on exposure to light of longer wavelengths (320–400 nm, UV A) produces a papular or eczematous contact dermatitis. Drugs involved are sulfonamides, sulfonylureas, griseofulvin, chloroquine, and chlorpromazine.
8. **Drug dependence:** Drug dependence is a state in which use of drugs for personal satisfaction is accorded a higher priority than other basic needs, often in the face of known risks to health.
 - a. **Psychological dependence:** It is said to have developed when the individual believes that optimal state of wellbeing is achieved only through the actions of the drug. For example, opioid, cocaine, benzodiazepines.
 - b. **Physical dependence:** It is an altered physiological state produced by repeated administration of a drug which necessitates the continued presence of the drug to maintain physiological equilibrium. For example, opioid, barbiturates, alcohol and benzodiazepines.
 - c. **Drug abuse:** It is the use of a drug by self-medication in a manner and amount that deviates from the approved medical and social patterns in a given culture at a given time.
 - d. **Drug addiction:** It is a pattern of compulsive drug use characterized by overwhelming involvement with the use of a drug. For example, amphetamines, cocaine, cannabis, LSD.
 - e. **Drug habituation:** It denotes less intensive involvement with the drug, so that its withdrawal produces only mild discomfort. For example, consumption of tea, coffee, tobacco, social drinking.
9. **Drug withdrawal reactions:** Sudden interruption of drug therapy may result in adverse consequences, e.g.
 - i. Acute adrenal insufficiency may be precipitated by abrupt cessation of corticosteroid therapy.
 - ii. Frequency of seizures may increase on sudden withdrawal of an antiepileptic.
10. **Teratogenicity:** It refers to capacity of a drug to cause fetal abnormalities when administered to the pregnant mother. The placenta does not strictly constitute a barrier and any drug can cross it to a

greater or lesser extent. The embryo is one of the most dynamic biological systems and in contrast to adults, drug effects are often irreversible. The thalidomide disaster (1958–61) resulting in thousands of babies born with phocomelia (seal-like limbs) and other defects focused attention to this type of adverse effect. Drugs can affect the fetus at 3 stages:

- i. *Fertilization and implantation (conception to 17 days)*: Failure of pregnancy which often goes unnoticed.
- ii. *Organogenesis (18–55 days of gestation)*: Most vulnerable period, deformities are produced.
- iii. *Growth and development (56 days onwards)*: Developmental and functional abnormalities can occur, e.g. ACE inhibitors can cause hypoplasia of organs, especially lungs and kidneys; NSAIDs may induce premature closure of ductus arteriosus. It is, therefore, wise to avoid all drugs during pregnancy unless compelling reasons exist for their use regardless of the assigned pregnancy category, or presumed safety. Frequency of spontaneous as well as drug-induced malformations, especially neural tube defects, may be reduced by folate therapy during pregnancy.

11. Mutagenicity and carcinogenicity: It refers to capacity of a drug to cause genetic defects and cancer respectively. Usually oxidation of the drug results in the production of reactive intermediates which affect genes and may cause structural changes in the chromosomes. Drugs implicated in these adverse effects are—anticancer drugs, radioisotopes, estrogens, tobacco.

12. Drug-induced diseases: These are also called **iatrogenic (physician induced) diseases**, and are functional disturbances (disease) caused by drugs which persist even after the offending drug has been withdrawn and largely eliminated, e.g. peptic ulcer by salicylates and corticosteroids, parkinsonism by phenothiazines and other antipsychotics.

Prevention of adverse effects to drugs

1. Avoid all inappropriate use of drugs.
2. Use appropriate dose, route and frequency of drug administration.
3. Elicit and take into consideration previous history of drug reactions.
4. Elicit history of allergic diseases.
5. Rule out possibility of drug interactions when more than one drug is prescribed.
6. Adopt correct drug administration technique.
7. Carry out appropriate laboratory monitoring.

Q. 8. Write a short note on drug reactions and interactions. (BFUHS, May 2010; TNMGR, Sept. 2010)

Ans. Drug interaction refers to modification of response to one drug by another when they are administered simultaneously or in quick succession. The response is either increased or decreased in intensity (quantitative), but sometimes an abnormal or a different type of response is produced (qualitative).

Types of drugs most likely to be involved in clinically important drug interactions

- Drugs with narrow safety margin, e.g. aminoglycoside antibiotics, digoxin, lithium.
- Drugs affecting closely regulated body functions, e.g. antihypertensive, antidiabetic, anticoagulants.
- Highly plasma protein bound drugs like NSAIDs, oral anticoagulants, sulfonylureas.
- Drugs metabolized by saturation kinetics, e.g. phenytoin, theophylline.

Mechanism of drug interactions: Drug interactions can be broadly divided into pharmacokinetic and pharmacodynamic interactions.

A. Pharmacokinetic interactions: These interactions alter the concentration of the object drug at its site of action by affecting its absorption, distribution, metabolism or excretion.

Pharmacokinetic interactions

- Alteration of absorption or first-pass metabolism.
- Displacement of plasma protein bound drug.
- Alteration of drug binding to tissues affecting volume of distribution and clearance.
- Inhibition/induction of metabolism.
- Alteration of excretion.

i. **Absorption:** Absorption of an orally administered drug can be affected by other concurrently ingested drugs. For example, tetracyclines and calcium/iron salts, antacids or sucralfate.

ii. **Distribution:** Interactions involving drug distribution are primarily due to displacement of one drug from its binding sites on plasma proteins by another drug. For example, quinidine reduce the binding of digoxin to tissue proteins by inhibiting the efflux transporter P-glycoprotein, resulting in nearly doubling of digoxin blood levels and toxicity.

iii. **Metabolism:** Certain drugs reduce or enhance the rate of metabolism of other drugs, e.g. macrolides, azole antifungal, chloramphenicol are inhibitors of metabolism of multiple drugs.

- iv. **Excretion:** Interaction involving excretion is important mostly in case of drugs actively secreted by tubular transport mechanisms, e.g. probenecid inhibits tubular secretion of penicillins and cephalosporins and prolongs their plasma $t_{1/2}$.

Selected clinically important drug interactions

1. Ampicillin interrupts enterohepatic circulation of the estrogen → failure of contraception.
2. Oral anticoagulants inhibits gut flora → decreased vit. K production in gut → risk of bleeding.
3. Ampicillin with allopurinol → increased incidence of rashes.
4. Metronidazole with alcohol → accumulation of acetaldehyde → disulfiram-like or bizarre reactions.
 - Precipitant drug is the drug, which alters the action/pharmacokinetics of the other drug.
 - Object drug is the drug whose action/pharmacokinetics is altered.

B. Pharmacodynamic interactions: These interactions derive from modification of the action of one drug at the target site by another drug, independent of a change in its concentration. This may result in an enhanced response (synergism), an attenuated response (antagonism) or an abnormal response. For example,

1. Sedation, respiratory depression, motor in coordination due to concurrent administration of a benzodiazepine and a sedating antihistaminic.
2. Excessive fall in BP and fainting due to concurrent administration of α_1 adrenergic blockers, vasodilators, ACE inhibitors, high ceiling diuretics and cardiac depressants.
3. Excessive platelet inhibition resulting in bleeding due to simultaneous use of aspirin/ticlopidine/clopidogrel and carbenicillin.
4. Increased risk of bleeding due to concurrent use of antiplatelet drugs with anticoagulants.

Drug interactions before administration: Certain *in vitro* interactions occur when injectable drugs are mixed in the same syringe or infusion bottle. Some examples are:

- Penicillin G or ampicillin mixed with gentamicin or another aminoglycoside antibiotic.
- Thiopentone sodium when mixed with succinylcholine or morphine.
- Heparin when mixed with penicillin/gentamicin/hydrocortisone.
- Noradrenaline when added to sodium bicarbonate solution.

In general, it is advisable to avoid mixing of any two or more parenteral drugs before injecting.

Recommendations

1. Not all patients taking interacting drugs experience adverse consequences.
2. Two drugs that have the potential to interact do not necessarily contraindicate their concurrent use.
3. Knowledge of the nature and mechanism of the possible interaction may permit their concurrent use provided appropriate dose adjustments are made or other corrective measures are taken.
4. It is prudent to consider the possibility of drug interaction whenever two or more drugs are prescribed to a patient, or any drug is added to what the patient is already taking.

Q. 9. Discuss the various factors modifying the actions of a drug in the human body. (TNMGR, Sept. 2009)

Ans. The various factors are discussed below:

1. **Body size:** It influences the concentration of the drug attained at the site of action. The average adult dose refers to individuals of medium built. For exceptionally obese or lean individuals and for children dose may be calculated on body weight (BW) basis:
 Individual dose = $\text{BW (kg)} / 70 \times \text{average adult dose}$
 Individual dose = $\text{BSA (m}^2\text{)} / 1.7 \times \text{average adult dose}$;
 Body surface area (BSA).
2. **Age:** The dose of a drug for children is often calculated from the adult dose.
 Child dose = $\text{Age} / \text{Age} + 12 \times \text{adult dose}$ (Young's formula).
 Child dose = $\text{Age} / 20 \times \text{adult dose}$ (Dilling's formula).
 In the elderly, renal function progressively declines so that GFR is ~ 75% at 50 years and ~ 50% at 75 years age compared to young adults. Drug doses have to be reduced.
3. **Sex:** Females have smaller body size and require doses that are on the lower side of the range. In women consideration must also be given to menstruation, pregnancy and lactation. Drugs given during pregnancy can affect the fetus.
4. **Species and race:** There are many examples of differences in responsiveness to drugs among different species. For example, Indians tolerate thiacezone better than whites.
5. **Genetics:** All key determinants of drug response, viz. transporters, metabolizing enzymes, ion channels, receptors with their couplers and effectors are controlled genetically. Hence, a great deal of individual variability can be traced to the genetic composition of the subject. The study of genetic basis for variability in drug response is called 'Pharmacogenetics'.
6. **Route of administration:** Parenteral administration is often resorted to for more rapid, more pronounced and more predictable drug action. A drug may have

entirely different uses through different routes, e.g. magnesium sulfate given orally causes purgation, applied on sprained joints—decreases swelling, while intravenously it produces CNS depression and hypotension.

7. **Environmental factors and time of administration:** Exposure to insecticides, carcinogens, tobacco smoke and consumption of charcoal broiled meat are well known to induce drug between drug ingestion and meals can alter drug absorption.

8. **Psychological factor:** Efficacy of a drug can be affected by patient's beliefs, attitudes and expectations. This is particularly applicable to centrally acting drugs.

Placebo is an inert substance which is given in the garb of a medicine. It works by psychological rather than pharmacological means and often produces responses equivalent to the active drug.

Nocebo is the converse of placebo, and refers to negative psychodynamic effect evoked by loss of faith in the medication and/or the physician. Nocebo effect can oppose the therapeutic effect of active medication.

9. **Pathological states:** Not only drugs modify disease processes, several diseases can influence drug disposition and drug action.

10. **Other drugs:** Drugs can modify the response to each other by pharmacokinetic or pharmacodynamic interaction between them.

11. **Accumulation:** Any drug will accumulate in the body if rate of administration is more than the rate of elimination.

12. **Tolerance:** It refers to the requirement of higher dose of a drug to produce a given response.

Drug tolerance may be natural or acquired. **Cross tolerance** is the development of tolerance to pharmacologically related drugs, e.g. alcoholics are relatively tolerant to barbiturates and general anesthetics. **Tachyphylaxis** is rapid development of tolerance when doses of a drug repeated in quick succession result in marked reduction in response.

Drug resistance refers to tolerance of micro-organisms to inhibitory action of antimicrobials, e.g. staphylococci to penicillin.

2. DRUGS ACTING ON RESPIRATORY SYSTEM

Q. 1. Write a short note on expectorants.

(TNMGR, Sept. 2002)

Ans. Expectorants (mucokinetics) are drugs believed to increase bronchial secretion or reduce its viscosity, facilitating its removal by coughing.

Classification

a. Bronchial secretion enhancers

1. **Sodium or potassium citrate:** Increase bronchial secretion by salt action.
2. **Potassium iodide:** Secreted by bronchial mucosa and can irritate the airway mucosa.
3. **Guiphenesin (glyceryl guaiacolate), balsam of tolu, vasaka:** Plant products; enhance bronchial secretion and mucocilliary function while being secreted by tracheobronchial glands.
4. **Ammonium chlorides:** They are nauseating—reflexly increases respiratory secretions.

b. Mucolytics

1. **Bromhexine:** It produces thin copious bronchial secretions by depolymerizing mucopolysaccharides and liberating lysosomal enzymes, leading to breakage of network of fibers in the sputum.
Side effects: Rhinorrhea, lacrimation, gastric irritation.
Dose: Bromhexine (8 mg) TDS, 4 mg/5 ml elixir.
2. **Ambroxol:** It is a metabolite of bromhexine with similar effects. *Dose:* 15–30 mg TDS.
3. **Acetylcysteine:** It opens disulfide bonds in mucoproteins present in sputum—makes it less viscid. It has to be administered directly into respiratory tract.
4. **Carbocysteine:** Action is similar to acetylcysteine, but administered orally (250–750 mg TDS).

Q. 2. Write a short note on atropine sulfate.

(TNMGR, Aug. 2004)

Ans. The prototype drug of anticholinergic drugs is highly selective for muscarinic receptors, but some of its synthetic substitutes do possess significant nicotinic blocking property.

Classification

Natural alkaloids: Atropine, hyoscine (scopolamine).

Pharmacological actions (atropine as prototype)

1. **CNS:** Atropine has an overall CNS stimulant action. Majority of the central actions are due to blockade of muscarinic receptors.
2. **CVS:** The most prominent effect of atropine is to cause tachycardia. It is due to blockade of M2 receptors on SA node. Atropine does not have any consistent or marked effect on BP.
3. **Eye:** Mydriasis, abolition of light reflex and cycloplegia.
4. **Smooth muscles:** Atropine causes bronchodilatation and reduces airway resistance. Atropine has relaxant action on ureter and urinary bladder; urinary retention can occur in older males with prostatic hypertrophy.

5. **Glands:** Atropine markedly decreases sweat, salivary, tracheobronchial and lacrimal secretion (M3 blockade). Atropine decreases secretion of acid, pepsin and mucus in the stomach.
6. **Body temperature:** Rise in body temperature occurs at higher doses.
7. **Local anesthetic:** Atropine has a mild anesthetic action on the cornea.

Pharmacokinetics: Atropine and hyoscine are rapidly absorbed from GIT. About 50% of atropine is metabolized in liver and rest is excreted unchanged in urine. It has a $t_{1/2}$ of 3–4 hours.

Atropine sulfate: 0.6–2 mg IM, IV (children 10 $\mu\text{g/kg}$), 1–2% topically in eye.

3. DRUGS ACTING ON CVS

Q. 1. Write a short note on beta blockers.

(TNMGR, Oct. 2000)

Ans. These drugs inhibit adrenergic responses mediated through receptors.

Classification

a. Nonselective (both β_1 and β_2 blockers)

1. **With intrinsic sympathomimetic activity:** Pindolol.
2. **Without intrinsic sympathomimetic activity:** Propranolol, sotalol, timolol.
3. **With additional α -blocking property:** Labetalol, carvedilol.

b. Cardioselective (β_1): Metoprolol, atenolol, acebutol, bisoprolol, esmolol, etc.

Pharmacological actions

1. **CVS:** Propranolol decreases heart rate, force of contraction and cardiac output. It has no direct effect on blood vessels. On prolonged administration BP gradually falls in hypertensive subjects.
2. **Respiratory tract:** Propranolol increases bronchial resistance by blocking β_2 receptors.
3. **CNS:** Forgetfulness, increased dreaming and nightmares.
4. **Local anesthetic:** Propranolol is as potent a local anesthetic.
5. **Metabolic:** Propranolol blocks adrenergically induced lipolysis.
6. **Skeletal muscle:** Propranolol inhibits adrenergically provoked tremor.
7. **Eye:** It reduces secretion of aqueous humor.
8. **Uterus:** Relaxation of uterus in response to β_2 agonists is blocked by propranolol.

Pharmacokinetics: Propranolol is well absorbed after oral administration, but has low bioavailability due to high first pass metabolism in liver.

Dose: Oral: 10 mg BD to 160 mg QID (average 40–160 mg/day).

Interactions

1. Additive depression of sinus node and AV conduction with digitalis and verapamil.
2. Propranolol delays recovery from hypoglycemia due to insulin and oral antidiabetic.
3. Phenylephrine, ephedrine and other α agonists present in cold remedies can cause marked rise in BP due to blockade of sympathetic vasodilatation.
4. Indomethacin and other NSAIDs attenuate the antihypertensive action of β blockers.
5. Cimetidine inhibits propranolol metabolism.

Q. 2. Write about potassium sparing diuretics.

(TNMGR, Oct. 1999)

Ans.

a. **Aldosterone antagonist:** Spironolactone, eplerenone.

b. **Inhibitors of renal epithelial Na^+ channel:** Trimerene, amiloride.

Mechanism of action: Spironolactone acts from the interstitial side of the tubular cell, combines with the mineralocorticoid receptor and inhibits the formation of aldosterone-induced proteins (AIPs), which promote Na^+ reabsorption and K^+ secretion, in a competitive manner. It increases Ca^{2+} excretion by a direct action on renal tubules.

Pharmacokinetics: The oral bioavailability of spironolactone is 75%. It is highly bound to plasma proteins and completely metabolized in liver; converted to active metabolites. The $t_{1/2}$ of spironolactone is 1–2 hours.

Dose: 25–50 mg BD–QID.

Use

1. **Edema:** It is more useful in cirrhotic and nephritic edema.
2. To counteract K^+ loss due to thiazide and loop diuretics.
3. Hypertension.
4. Congestive heart failure (CHF).

Interactions

1. Given together with K^+ supplements—dangerous hyperkalemia can occur.
2. Aspirin blocks spironolactone action.
3. More pronounced hyperkalemia can occur in patients receiving ACE inhibitors/angiotensin receptor blockers (ARBs).

4. Spironolactone increases plasma digoxin concentration.

Adverse effects: Drowsiness, confusion, abdominal upset, hirsutism, gynecomastia, impotence and menstrual irregularities, hyperkalemia, acidosis.

Inhibitors of renal epithelial Na^+ channel: Their most important effect is to decrease K^+ excretion, particularly when it is high due to large K^+ intake or use of a diuretic that enhances K^+ loss.

Mechanism of action: The luminal membrane of late distal tubule and collecting duct cells expresses a distinct 'amiloride sensitive' or 'renal epithelial' Na^+ channel through which Na^+ enters the cell down its electrochemical gradient which is generated by Na^+/K^+ ATPase operating at the basolateral membrane. This Na^+ entry partially depolarizes the luminal membrane creating transepithelial potential difference which promotes secretion of K^+ into the lumen through K^+ channels. Amiloride and triamterene block the luminal Na^+ channels—indirectly inhibit K^+ excretion, while the net excess loss of Na^+ is minor.

Q. 3. Write a short note on drugs in myocardial infarction. (TNMGR, Sept. 2002)

Ans. Myocardial infarction (MI) is ischemic necrosis of a portion of the myocardium due to sudden occlusion of a branch of coronary artery. An acute thrombus at the site of atherosclerotic obstruction is the usual cause. The drug therapy for MI can be directed to:

1. **Pain, anxiety and apprehension:** Opioid analgesics (morphine/pethidine), diazepam administered parenterally.
2. **Oxygenation:** By O_2 inhalation and assisted respiration, if needed.
3. **Maintenance of blood volume, tissue perfusion and microcirculation:** Slow IV infusion of saline/low molecular weight dextran (avoid volume overload).
4. **Correction of acidosis:** Due to lactic acid production: Sodium bicarbonate by IV infusion.
5. **Prevention and treatment of arrhythmias:** Prophylactic IV infusion of a β blocker. Tachyarrhythmias may be treated with lidocaine, procainamide or other antiarrhythmics. Bradycardia and heart block may be managed with atropine or electrical pacing.
6. **Pump failure:** The objective is to increase cardiac output and/or decrease filling pressure without unduly increasing cardiac work or reducing BP. Drugs used for this purpose are:
 - a. **Furosemide:** It decreases cardiac preload.
 - b. **Vasodilators:** Venous or combined dilator is selected according to the monitored hemo-

dynamic parameters. Drugs like glyceryl trinitrate (GTN) IV or nitroprusside have been mainly used.

- c. **Inotropic agents:** Dopamine or dobutamine may be needed to augment the pumping action of heart and tide over the crisis.
7. **Prevention of thrombus extension, embolism, and venous thrombosis:** Aspirin (162–325 mg) should be given for chewing and swallowing as soon as MI is suspected. This is continued at 80–160 mg/day. Anti-coagulants (heparin followed by oral anticoagulants) are used primarily to prevent deep vein thrombosis and pulmonary/systemic arterial embolism.
 8. **Thrombolysis and reperfusion:** Fibrinolytic agents, i.e. plasminogen activators—streptokinase/urokinase/alteplase to achieve reperfusion of the infarcted area.
 9. **Prevention of remodeling and subsequent CHF:** ACE inhibitors/angiotensin receptor blockers (ARBs) are of proven efficacy and afford long-term survival benefit.
 10. **Prevention of future attacks**
 - a. **Platelet inhibitors:** Aspirin or clopidogrel given on long-term basis is routinely prescribed.
 - b. **β -blockers:** Reduce risk of reinfarction, CHF and mortality. All patients not having any contra-indication are put on β blocker for at least 2 years.
 - c. **Control of hyperlipidemia:** Dietary substitution with unsaturated fats, hypolipidemic drugs especially statins.

Q. 4. Write about role of diuretics in hypertension.

(TNMGR, Sept. 2002)

Ans. Thiazides and related drugs (chlorthalidone, etc.) are the diuretic of choice in uncomplicated hypertension. The proposed mechanism of antihypertensive action is:

1. Initially, the diuresis reduces plasma and extracellular fluid (ECF) volume by 5–15% → decreased cardiac output.
2. Subsequently, compensatory mechanisms operate to almost regain Na^+ balance and plasma volume; cardiac output is restored, but the fall in BP is maintained.
3. The reduction in total peripheral resistance (TPR) is most probably an indirect consequence of a small persisting Na^+ and volume deficit.

They are indicated in hypertension only when it is complicated by

- a. **Chronic renal failure:** Thiazides are ineffective, both as diuretics and antihypertensives.
- b. **Coexisting refractory CHF.**

- c. Resistance to combination regimens containing a thiazide, or marked fluid retention due to use of potent vasodilators.

Desirable properties of diuretics as antihypertensives are

1. Once a day dosing
2. No fluid retention, no tolerance.
3. Low incidence of postural hypotension and relative freedom from side effects, especially CNS, compared to sympatholytics.
4. Effective in isolated systolic hypertension (ISH).
5. Lessened risk of hip fracture in the elderly due to hypocalciuric action of thiazides.
6. Low cost.

Potassium sparing diuretics: Spironolactone or amiloride themselves lower BP slightly, but they are used only in conjunction with a thiazide diuretic to prevent K^+ loss and to augment the antihypertensive action.

Q. 5. Write a short note on furosemide.

(TNMGR, Oct. 2003)

Ans. High ceiling diuretic (inhibitors of $Na^+-K^+-2Cl^-$ cotransport): Furosemide (20–80 mg oral or IV). It may be given as an adjunct with drugs if there is volume overload (acute LVF, pulmonary edema, CHF) or cerebral edema (in encephalopathy), but should be avoided when patient may be hypovolemic due to pressure induced natriuresis.

The onset of action is prompt and duration short (3–6 hours). The major site of action is the thick ascending limb of loop of Henle, where furosemide inhibits $Na^+-K^+-2Cl^-$ cotransport.

It is secreted in proximal tubule by organic anion transport and reaches ascending limb of loop of Henle, where it acts from luminal side of the membrane. It abolishes the corticomedullary osmotic gradient and blocks positive as well as negative free water clearance. K^+ excretion is increased mainly due to high Na^+ load reaching distal tubule.

Intravenous furosemide causes prompt increase in systemic venous capacitance and decreases left ventricular filling pressure, and are responsible for the quick relief it affords in left ventricular failure (LVF) and pulmonary edema.

Pharmacokinetics: Furosemide is rapidly absorbed orally but bioavailability is about 60%. It is highly bound to plasma proteins. It is partly conjugated with glucuronic acid and mainly excreted unchanged by glomerular filtration as well as tubular secretion. Plasma $t_{1/2}$ averages 1–2 hours.

Dose: Usually 20–80 mg once daily in the morning.

Use of high ceiling diuretics

1. Edema.
2. Acute pulmonary edema (acute LVF, following MI).
3. Cerebral edema.
4. Hypertension.
5. Along with blood transfusion in severe anemia, to prevent vascular overload.
6. Hypercalcemia and renal calcium stones.

Q. 6. Write a short note on calcium channel blockers.

(TNMGR, March 2009)

Ans. Three important classes of calcium channel blockers (CCBs) are exemplified by:

Verapamil: Phenyl alkylamine, hydrophilic papaverine congener.

Nifedipine: Dihydropyridine (lipophilic).

Diltiazem: Hydrophilic benzothiazepine.

The dihydropyridines (DHPs) are the most potent Ca^{2+} channel blockers.

Pharmacological actions and adverse effects: The common property of all three subclasses of CCBs is to inhibit Ca^{2+} mediated slow channel component of action potential (AP) in smooth/cardiac muscle cell. The two most important actions of CCBs are:

- i. Smooth muscle (especially vascular) relaxation.
- ii. Negative chronotropic, inotropic and dromotropic actions on heart.

4. DRUGS ACTING ON CNS

Q. 1. Explain the pharmacological basis for phenytoin sodium in grandmal epilepsy. (TNMGR, April 2001)

Ans. Grandmal epilepsy is also known as generalized tonic-clonic seizures. It is a major form of generalized seizures. It is the commonest of all seizures and last for 1–2 minutes. The usual sequence is aura → cry → unconsciousness → tonic spasm of all body muscles → clonic jerking → prolonged sleep → depression of all CNS functions.

Phenytoin (diphenylhydantoin): The most outstanding action is abolition of tonic phase of maximal electroshock seizures, with no effect on or prolongation of clonic phase. It limits spread of seizure activity.

Mechanism of action: Phenytoin has a stabilizing influence on neuronal membrane, prevents repetitive detonation of normal brain cells during 'depolarization

shift' that occurs in epileptic patients. This is achieved by prolonging the inactivated state of voltage sensitive neuronal Na^+ channel that governs the refractory period of the neuron. As a result high frequency discharges are inhibited.

Pharmacokinetics: Absorption of phenytoin by oral route is slow. It is widely distributed in the body and is 80–90% bound to plasma proteins. Phenytoin is metabolized in liver by hydroxylation and glucuronide conjugation. The $t_{1/2}$ (12–24 hours) progressively increases (up to 60 hrs) when plasma concentration rises above 10 $\mu\text{g}/\text{ml}$. Only 5% unchanged phenytoin is excreted in urine.

Adverse effects

At therapeutic levels (5H)

- Gum hypertrophy
- Hirsutism
- Hypersensitivity reactions
- Megaloblastic anemia
- Osteomalacia
- Hyperglycemia
- Fetal hydantoin syndrome

At high plasma levels (dose related toxicity)

- Cerebellar and vestibular manifestations.
- Drowsiness, behavioral alterations, mental confusion, hallucinations, disorientation and rigidity.
- Epigastric pain, nausea and vomiting.
- Intravenous injection can cause local vascular injury.
- Fall in BP and cardiac arrhythmias occur only on IV injection.

Uses: Phenytoin is a first line antiepileptic drug for:

- Generalized tonic-clonic, simple and complex partial seizures. It is ineffective in absence seizures. **Dose:** 100 mg BD, maximum 400 mg/day; children 5–8 mg/kg/day.
- Status epilepticus.
- Trigeminal neuralgia.

Q. 2. Explain the pharmacological basis for the sodium thiopentone as including agent for general anesthesia. (TNMGR, April 2001; BFUHS, Oct. 2010)

Ans. It is an ultra short acting thiobarbiturate, highly soluble in water. Injected IV (3–5 mg/kg) as a 2.5% solution, it produces unconsciousness in 15–20 sec. Its undissociated form has high lipid solubility, enters brain almost instantaneously. Initial distribution depends on organ blood flow—brain gets large amounts. However, as other less vascular tissues gradually take up the drug, blood concentration falls

and it back diffuses from the brain: Consciousness is regained in 6–10 min ($t_{1/2}$ of distribution phase is 3 mins). On repeated injection, the extracerebral sites are gradually filled up, lower doses produce anesthesia which lasts longer. Its ultimate disposal occurs mainly by hepatic metabolism (elimination $t_{1/2}$ is 7–12 hr).

Thiopentone is a poor analgesic. Painful procedures should not be carried out under its influence unless an opioid or N_2O has been given; otherwise, the patient may struggle, shout and show reflex changes in BP and respiration. It is a weak muscle relaxant; does not irritate air passages. Respiratory depression with inducing doses of thiopentone is generally transient. Cardiovascular collapse may occur if hypovolemia, shock or sepsis is present. It does not sensitize the heart to adrenaline, arrhythmias are rare. Thiopentone is a commonly used inducing agent. It can be employed as the sole anesthetic for short operations that are not painful.

Q. 3. Write about clinical uses of muscle relaxants.

(TNMGR, Nov. 2001)

Q. Write a short note on muscle relaxants.

Ans. Skeletal muscle relaxants are drugs that act peripherally at neuromuscular junction/muscle fiber itself or centrally in the cerebrospinal axis to reduce muscle tone and/or cause paralysis.

Peripherally Acting Muscle Relaxants

I. Neuromuscular blocking agents

a. Nondepolarizing (competitive) blockers

- Long acting: d-tubocurarine, pancuronium, doxacurium, pипеcuronium.
- Intermediate acting: Vecuronium, atracurium, cisatracurium, rocuronium, rapacurium.
- Short acting: Mivacurium.

b. Depolarizing blockers: Succinylcholine (SCh), suxamethonium, decamethonium.

II. Directly acting agents

- Dantrolene sodium
- Quinine

Uses

- The most important use of neuromuscular blockers is as adjuvant to general anesthesia.
- Assisted ventilation:** Competitive neuromuscular blocker which reduces the chest wall resistance to inflation.
- Convulsions and trauma from electroconvulsive therapy can be avoided by the use of muscle relaxants.
- Severe cases of tetanus and status epilepticus may be paralyzed by a neuromuscular blocker.

Centrally Acting Muscle Relaxants

They selectively depress spinal and supraspinal polysynaptic reflexes involved in the regulation of muscle tone without significantly affecting mono-synaptically mediated stretch reflex.

Classification

- i. Mephenesin congeners: Mephenesin, carisoprodol, chlorzoxazone, chlormezanone, methocarbamol.
- ii. Benzodiazepines: Diazepam and others.
- iii. GABA derivative: Baclofen.
- iv. Central α_2 agonist: Tizanidine

Uses of centrally acting muscle relaxants

1. Acute muscle spasms.
2. Torticollis, lumbago, backache, neuralgias.
3. Anxiety and tension.
4. Spastic neurological diseases.
5. Tetanus.
6. Electroconvulsive therapy.
7. Orthopedic manipulations.

Q. 4. Write a short note on tricyclic antidepressants (TCAs). (TNMGR, Oct. 2012)

Ans.

Classification

- a. **NA+5-HT reuptake inhibitors:** Imipramine, amitriptyline, trimipramine, doxepin, dothiepin, Clomipramine.
- b. **Predominantly NA reuptake inhibitors:** Desipramine, nortriptyline, amoxapine, reboxetine.

Pharmacological actions: The most prominent action of TCAs is their ability to inhibit norepinephrine transporter (NET) and serotonin transporter (SERT) located at neuronal/platelet membrane at low and therapeutically attained concentrations. The TCAs inhibit monoamine reuptake and interact with a variety of receptors, viz. muscarinic, α -adrenergic, histamine H_1 , 5-HT₁, 5-HT₂ and occasionally dopamine D₂.

The actions of imipramine are described as prototype.

1. CNS

In normal individuals: It induces clumsy feeling, tiredness, light-headedness, and sleepiness, difficulty in concentrating and thinking, unsteady gait.

In depressed patients: A little acute effects. After 2–3 weeks of continuous treatment, the mood is gradually elevated; patients become more communicative and start taking interest in self and surroundings.

Mechanism of action: Inhibition of noradrenaline (NA) and 5-hydroxytryptamine (5-HT) uptake is associated with antidepressant action.

2. **ANS:** Most TCAs are potent anticholinergics—causes dry mouth, blurring of vision, constipation and urinary hesitancy.
3. **CVS:** Tachycardia, postural hypotension, T wave suppression or inversion, cardiac arrhythmias.

Tolerance and dependence: Tolerance to the anticholinergic and hypotensive effects of imipramine-like drugs develops gradually, though antidepressant action is sustained.

Psychological dependence on these drugs is rare.

Pharmacokinetics: The oral absorption of TCAs is good. They are extensively metabolized in liver. Metabolites are excreted in urine over 1–2 weeks. The plasma $t_{1/2}$ of range between 16 and 24 hours.

Adverse Effects

1. **Anticholinergic:** Dry mouth, bad taste, constipation, epigastric distress, urinary retention, blurred vision, palpitation.
2. Sedation, mental confusion and weakness.
3. Increased appetite and weight gain.
4. Dysphoric agitated state or mania.
5. Sweating and fine tremors.
6. Seizure threshold is lowered—fits may be precipitated.
7. Postural hypotension.
8. Cardiac arrhythmias.
9. Rashes and jaundice.

Q. 5. Write a short note on use of diazepam in dentistry. Mention also the contradictions. (BFUHS, Nov. 2009)

Ans. Diazepam is a benzodiazepine, which act on central nervous system (CNS).

Mechanism of action: It binds to GABA_A-receptor Cl⁻ channel complex and potentiates the inhibitory effect of GABA, which increases the frequency of opening of Cl⁻ channels. This leads to increase in chloride conductance, membrane hypopolarization leading to CNS depression.

Uses

1. For sedation and hypnosis.
2. As anticonvulsant.
3. During diagnostic and minor operative procedures.
4. In conscious sedation.
5. In preanesthetic medication.
6. As antianxiety.
7. Muscle relaxant.
8. To treat alcohol withdrawal symptoms.

Side-effects: Drowsiness, confusion, blurred vision, amnesia, disorientation, tolerance and drug dependence. It may cause respiratory depression and hypotonia in the newborn (floppy baby syndrome), if used during pregnancy.

Contraindications: Hypersensitivity to benzodiazepines, myasthenia gravis.

Q. 6. Write about the objectives of preanesthetic medication?

(TNMGR, Nov. 1995, March 2007, April 2012, 2015; BFULS, Oct. 2010)

Q. Write a short note on preanesthetic medication and add a note on ketamine anesthesia.

(TNMGR, April 2012)

Ans. Preanesthetic medication is defined as use of drugs before anesthesia to make it more pleasant and safe. The objectives of preanesthetic medication are:

1. Relief of anxiety and apprehension preoperatively.
2. To facilitate smooth induction.
3. Amnesia for pre- and postoperative events.
4. To supplement and potentiate the analgesic action of anesthetics, so that less anesthetic is needed.
5. To decrease secretions, vagal stimulation caused by anesthetics.
6. Antiemetic effect which extends postoperatively.
7. To decrease acidity and amount of gastric secretions so that it is less damaging, if aspirated.

Drugs used for preanesthetic medication

1. **Sedative-anxiety drugs:** Benzodiazepines like diazepam (5–10 mg oral), lorazepam (2 mg or 0.05 mg/kg IM 1 hr before), midazolam (IV), and antihistaminic like promethazine (50 mg IM).
2. **Opioids:** Morphine (10 mg) or pethidine (50–100 mg) IM. Because of side effects of opioids, their use is highly restricted to those having preoperative pain.
3. **Anticholinergics:** Atropine or hyoscine (0.6 mg IM/IV), glycopyrrolate (0.1–0.3 mg IM).
4. **Neuroleptics:** Chlorpromazine (25 mg), trifluoperazine (10 mg), or haloperidol (2–4 mg) IM.
5. **H₂ blockers:** Ranitidine (150 mg), or famotidine (20 mg), omeprazole or pantoprazole (20 mg).
6. **Antiemetics:** Metoclopramide (10–20 mg IM), domperidone, selective 5 HT₃ blocker ondansetron (4–8 mg IV).

Q. 7. Write a short note on ultra-short acting barbiturates.

(TNMGR, April 1998)

Ans. Classification of barbiturates

1. **Ultra-short acting:** Thiopentone, methohexitone.
2. **Short acting:** Butobarbitone, phenobarbitone.

3. **Long acting:** Phenobarbitone.

Barbiturates are substituted derivatives of barbituric acid (malonyl urea). Barbiturates have variable lipid solubility; the more soluble ones are more potent and shorter acting.

Pharmacological actions: Barbiturates are general depressants for all excitable cells, the CNS is most sensitive.

1. **CNS:** Barbiturates produce dose-dependent effects: Sedation → sleep → anaesthesia → coma.

Mechanism of action

- i. Barbiturates appear to act primarily at the GABA: BZD receptor-Cl⁻ channel complex and potentiate GABAergic inhibition by increasing the lifetime of Cl⁻ channel opening induced by GABA. (Contrast BZDs which enhance frequency of Cl⁻ channel opening.)
- ii. At high concentrations, barbiturates directly increase Cl⁻ conductance (GABA-mimetic action; contrast BZDs which have only GABA-facilitatory action) and inhibit Ca²⁺ dependent release of neurotransmitters.
- iii. At very high concentrations, barbiturates depress voltage sensitive Na⁺ and K⁺ channels as well.

Other systems: Respiration is depressed by relatively higher doses.

2. **CVS:** Decrease in BP and heart rate, reflex tachycardia.

3. **Skeletal muscle:** Reduce muscle contraction.

4. **Smooth muscles:** Tone and motility of bowel are decreased.

5. **Kidney:** Barbiturates tend to reduce urine flow by decreasing BP and increasing antidiuretic hormone release.

Pharmacokinetics: Barbiturates are well absorbed from the gastrointestinal tract. The rate of entry into CNS is dependent on lipid solubility. Barbiturates cross placenta and are secreted in milk; can produce effects on the fetus and suckling infant.

Uses

1. **Epilepsy:** Phenobarbitone.
2. **Anesthesia:** Thiopentone.
3. As hypnotic and anxiolytic (rarely).
4. As adjuvant in psychosomatic disorders.
5. Congenital nonhemolytic jaundice and kernicterus.

Side effects

1. Hangover.
2. Tolerance and dependence.

3. Mental confusion, impaired performance and traffic accidents.
4. Idiosyncrasy.
5. Precipitation of porphyria.
6. Hypersensitivity rashes, swelling of eyelids, lips, etc.

Contraindications

1. Acute intermittent porphyria.
2. Liver and kidney disease.
3. Severe pulmonary insufficiency.
4. Obstructive sleep apnea.

Q. 8. Write a short note on lignocaine.

(TNMGR, April 2012; KUHS, Jan., 2014)

Q. Classify local anesthetics and its mechanism of action. Describe the various anesthetic techniques employed to achieve pulpal anesthesia.

(TNMGR, Oct. 2000, Sept. 2008; RGUHS, Oct. 2010)

Q. Discuss the pharmacology of anesthetic drugs used in dental practice.

(TNMGR, April 1995)

Q. Write a short note on vasoconstrictors in local anesthesia.

(RGUHS, May 2011)

Q. Write a short note on topical anesthetics.

(TNMGR, Sept. 2007)

Q. Discuss techniques of local anesthesia. Enumerate types of local anesthetic agents.

Ans.

Classification

a. Injectable anesthetic

- i. Low potency, short duration: Procaine, chlorprocaine.
- ii. Intermediate potency and duration: Lidocaine (lignocaine), prilocaine.
- iii. High potency, long duration: Tetracaine (amethocaine), bupivacaine, ropivacaine, dibucaine (cinchocaine).

b. Surface anesthetic

- i. Soluble insoluble
- ii. Cocaine benzocaine
- iii. Lidocaine butylaminobenzoate
- iv. Tetracaine
- v. Benoxinate oxethazaine

Classification (Structure Based)

1. **Esters:** Cocaine, procaine, chlorprocaine, benzocaine, tetracaine.
2. **Amides:** Lignocaine, mepivacaine, bupivacaine, prilocaine, ropivacaine.

Mechanism of action: The local anesthetics (LAs) block nerve conduction by decreasing the entry of Na^+ ions during upstroke of action potential (AP). As the concentration of the LA is increased, the rate of rise of AP and maximum depolarization decreases, causing slowing of conduction. Finally, local depolarization fails to reach the threshold potential and conduction block ensues. The LAs interact with a receptor situated within the voltage sensitive Na^+ channel and raise the threshold of channel opening, Na^+ permeability fails to increase in response to an impulse or stimulus. The equilibrium between the unionized base form (B) and the ionized cationic form (BH^+) depends on the pK_a of the LA. The predominant active species (cationic form of LA) is able to approach its receptor only when the channel is open at the inner face and it binds more avidly to the inactive state of the channel, prolonging the inactive state. The channel takes longer to recover refractory period of the fiber is increased.

a. Local actions: The clinically used LAs have no/minimal local irritant action and block sensory nerve endings, nerve trunks, neuromuscular junction, ganglionic synapse and receptors (non-selectively). They also reduce release of acetylcholine from motor nerve endings. Sensory and motor fibers are inherently equally sensitive. Myelinated nerves are blocked earlier than nonmyelinated. Smaller fibers are more sensitive than larger fibers. Sensory fibers are more vulnerable than the motor fibers. Autonomic fibers are generally more susceptible than somatic fibers. Among the somatic afferents order of blockade is, pain-temperature sense-touch-deep pressure sense. In general, fibers that are more susceptible to LA are the first to be blocked and the last to recover. Nerve sheaths restrict diffusion of the LA into the nerve trunk so that fibers in the outer layers are blocked earlier than the inner or core fibers. As a result, the more proximal areas supplied by a nerve are affected earlier. In a mixed nerve, motor fibers are usually present circumferentially; may be blocked earlier than the sensory fibers in the core of the nerve.

The LA often fails to afford adequate pain control in inflamed tissues (like infected tooth). The likely reasons are:

- a. Inflammation lowers pH of the tissue—greater fraction of the LA is in the ionized form hindering diffusion into the axolemma.
- b. Blood flow to the inflamed area is increased—the LA is removed more rapidly from the site.
- c. Effectiveness of adrenaline (Adr) injected with the LA is reduced at the inflamed site.
- d. Inflammatory products may oppose LA action.

Addition of a vasoconstrictor: For example, adrenaline (1:50,000 to 1:200,000):

- Prolongs duration of action of LAs by decreasing their rate of removal from the local site into the circulation.
- Enhances the intensity of nerve block.
- Reduces systemic toxicity of LAs: Rate of absorption is reduced and metabolism keeps the plasma concentration lower.
- Makes the injection more painful.
- Provides a more bloodless field for surgery.
- Increases the chances of subsequent local tissue edema and necrosis as well as delays wound healing by reducing oxygen supply and enhancing oxygen consumption in the affected area.
- May raise BP and promote arrhythmia in susceptible individuals.

b. Systemic actions: Any LA injected or applied locally is ultimately absorbed and can produce systemic effects depending on the concentration attained in the plasma and tissues.

1. **CNS:** There is a sequence of stimulation followed by depression. Euphoria—excitement—mental confusion—restlessness—tremor and twitching of muscles—convulsions—unconsciousness—respiratory depression—death, in a dose-dependent manner.
2. **CVS**
 - i. **Heart:** LAs at high doses or on inadvertent IV injection, they decrease automaticity, excitability, contractility, conductivity and increase effective refractory period (ERP).
 - ii. **Blood vessels:** LAs tend to produce fall in BP.

Pharmacokinetics: Soluble surface anesthetics (lidocaine, tetracaine) are rapidly absorbed from mucous membranes and abraded areas. The absorbed LA being lipophilic is widely distributed; rapidly enters highly perfused brain, heart, liver, and kidney, followed by muscle and other viscera. Ester-linked LAs (procaine, etc.) are rapidly hydrolyzed by plasma pseudocholinesterase and the remaining by esterase in the liver. Amide-linked LAs (lidocaine, etc.) are degraded only in the liver microsomes by dealkylation and hydrolysis. Metabolism of lidocaine is hepatic blood-flow dependent.

Adverse effects: Systemic toxicity on rapid IV injection is related to the intrinsic anesthetic potency of the LA. However, toxicity after topical application or regional injection is influenced by relative rates of absorption and metabolism; those rapidly absorbed but slowly metabolized are more toxic.

Lidocaine (lignocaine): It is a versatile LA, good both for surface application as well as injection and is available in a variety of forms. Injected around a nerve it blocks conduction within 3 mins. Also anesthesia is more intense and longer lasting. Vasodilatation occurs in the injected area. It is used for surface application, infiltration, nerve block, epidural, spinal and intravenous regional block anesthesia. In contrast to other LAs, early central effects of lidocaine are drowsiness, mental clouding, altered taste and tinnitus. Overdose causes muscle twitching, convulsions, cardiac arrhythmias, fall in BP, coma and respiratory arrest like other LAs. Lidocaine is popular antiarrhythmics.

Techniques of Local Anesthesia

1. **Surface anesthesia (topical anesthesia):** LA is applied on the abraded skin, mucous membrane. Tetracaine 2%, lignocaine 2–10%, cocaine 1–4%, benzocaine 1–2%. They are available as solutions, ointments, gel, cream, spray, lozenges, etc.
2. **Infiltration anesthesia:** LA is directed into tissues to be operated, it blocks sensory nerve endings. LA is infiltrated into the skin, subcutaneous tissue or deeper structures. The most frequently used LAs are lignocaine (0.5–1%), procaine (0.5–1%), bupivacaine (0.125–0.25%). It is suitable only for small areas. It can be used for drainage of an abscess, excision of small swelling, suturing of cut wounds, before root canal treatment. It is contraindicated if there is local infection and clotting disorders.
3. **Field block anesthesia:** It is achieved by injecting the LA subcutaneously which anaesthetize the area distal to the injection. This principle is used to in cases of minor procedures of scalp, anterior abdominal wall, extremities, teeth.
4. **Nerve block anesthesia:** LA is injected very close to or around the peripheral nerve or nerve plexuses. It produces larger areas of anesthesia than field block. In this, the requirement of LA is less than field block/infiltration.
 - a. **Maxillary nerve block**—for palatal, buccal and pulpal procedure in one quadrant.
 - b. **Anterior superior nerve block**—anterior teeth in one quadrant.
 - c. **Middle superior alveolar nerve block**—premolars in on quadrant.
 - d. **Inferior alveolar nerve block**—mandibular teeth in one quadrant.
 - e. **Buccal nerve block**—buccal soft tissue in the mandibular molar region.

5. **Spinal anesthesia:** LA is injected into the sub-arachnoid space to anaesthetize spinal roots. It is injected into the space between L2–3 and L3–4. Agents used are lignocaine, tetracaine, Bupivacaine, etc. It is used for surgical procedures below the level of umbilicus. Advantages are no loss of consciousness, good muscle relaxation, good analgesia. Complications are headache, hypotension, respiratory paralysis, septic meningitis, nerve injury.
6. **Epidural anesthesia:** LA is injected into epidural space where it acts on spinal nerve roots. It is safer but the technique is a little difficult than spinal anesthesia. It is slower in onset, require much larger doses. It is mainly used in obstetric analgesia.
7. **Intravenous regional anesthesia:** It is mainly used in anaesthetizing the upper limb. LA is injected into the vein of the limb whose blood flow is occluded by a tourniquet.

Q. 9. Write about merits and demerits of procaine.

(TNMGR, April 2000)

Ans. Procaine is low potency, short duration injectable anesthetic agent. It is the first synthetic local anesthetic introduced in 1905. Its popularity declined after the introduction of lidocaine: Practically not used now. It is not a surface anesthetic. It is derivatives of para-aminobenzoic acid. Procaine forms poorly soluble salt with benzyl penicillin; procaine penicillin injected IM acts for 24 hours due to slow absorption from the site of injection.

Merits

1. It is a nonirritant.
2. As effective as cocaine as local anesthetic.
3. Much less toxic.
4. Does not produce drug dependence.
5. Compatible in solutions with all vasoconstrictor.
6. It aids in breaking arteriospasm.
7. Safe in patients with hepatic dysfunction.

Demerits

1. Less potent than other.
2. Can reduce the effectiveness of sulfonamides.
3. Poor diffusion through interstitial tissue.
4. Because of extreme vasodilating property, chances of more bleeding.
5. Slow clinical onset of anesthesia.

Q. 10. Write on stages of general anesthesia.

(BFUHS, May 2010)

Ans. General anesthesia (GA) is a drug-induced loss of consciousness during which the patient is not

arousable, even by painful stimuli, accompanied by complete loss of protective reflexes including the ability to independently maintain ventilator function and respond purposefully to physical stimulation to physical stimulation or verbal command.

Stages of General Anesthesia

- i. **Stage of analgesia:** Starts from beginning of anesthetic inhalation and lasts up to the loss of consciousness. Pain is progressively abolished. Patient remains conscious, can hear and see, and feels a dream-like state; amnesia develops by the end of this stage. Reflexes and respiration remain normal.
- ii. **Stage of delirium:** From loss of consciousness to beginning of regular respiration. Apparent excitement is seen—patient may shout, struggle and hold his breath; muscle tone increases, jaws are tightly closed, breathing is jerky; vomiting, involuntary micturition or defecation may occur. Heart rate and BP may rise and pupils dilate due to sympathetic stimulation.
- iii. **Surgical anesthesia:** Extends from onset of regular respiration to cessation of spontaneous breathing. This has been divided into 4 planes:
Plane 1: Roving eyeballs. This plane ends when eyes become fixed.
Plane 2: Loss of corneal and laryngeal reflexes.
Plane 3: Pupil starts dilating and light reflex is lost.
Plane 4: Intercostal paralysis, shallow abdominal respiration, dilated pupil.
- iv. **Medullary paralysis:** Cessation of breathing to failure of circulation and death. Pupil is widely dilated, muscles are totally flabby, pulse is thready or imperceptible and BP is very low.

Q. 11. Write a short note on conscious sedation.

(BFUHS, May 2008)

Ans. Conscious sedation is defined as a state of altered consciousness that allows the patient to retain his airway and protective reflexes and respond appropriately to physical stimulation and/or verbal command.

Agents commonly used for conscious sedation are

a. Inhalation agents: Nitrous oxide and oxygen.

b. Systemic agents

i. *Conventional*

1. Lytic cocktail
2. Barbiturates: For example, phenobarbitone
3. Chloral hydrate.
4. Antihistaminic: For example, promethazine, hydroxyzine.
5. Benzodiazepines: For example, diazepam.

ii. *Contemporary*

1. *Newer benzodiazepines:* For example, midazolam, triazolam.
2. *Newer antihistaminic:* For example, loratidine.

Routes of drug administration for conscious sedation:

Oral, rectal, inhalational, submucosal, intramuscular, intravenous.

Indications for conscious sedation

1. Uncooperative patient.
2. Anxious patient.
3. Emotionally unstable patient.

It should be avoided in chronic obstructive pulmonary diseases, pregnancy, prolonged surgery, psychoses.

1. **Nitrous oxide:** It is delivered by means of flow meter utilizing nasal mask or hoods.

Advantages

1. Easy to administer.
2. Dose can be controlled.
3. Patient remains calm and relax.
4. Minimum side effects.

Concentration used during various stages

1. **Induction:** Slow: 0.5–1 L/min rapid: 2–4 L/min 40% nitrous oxide and 60% oxygen.
2. **Maintenance:** 20–30% nitrous oxide.
3. **Reversal:** 100% oxygen.

Effects on body

1. CNS depressant action.
2. Decreases cardiac output.
3. Increases peripheral resistance.
4. May cause respiratory depression.

2. **Diazepam:** It is lipid soluble, rapidly absorbed and reaches peak level within 2 hours. Its biotransformation is slow with half-life of 20–40 hours. It is redistributed in 30–40 minutes. It has anticonvulsant action too. It can be administered by oral, intramuscular, intranasal, subcutaneous route. When use by IV, injected slowly, as there is risk of thrombophlebitis. Ataxia and prolonged CNS depression are important side effects.

Dose: Oral/rectal: 0.2–0.5 mg/kg. IV: 0.25 mg/kg.

3. **Midazolam:** It is twice as potent as diazepam. It is water soluble, so less thrombophlebitis, sedation occurs within 3–5 minutes. Side effects include respiratory depression, hypertension.

Dose: Adult: 0.1–0.15 mg/kg. Pediatric: 0.05–0.1 mg/kg.

4. **Chloral hydrate:** It is a derivative of alcohol, can be given orally or rectally. Onset of action is within 15–30 minutes. Drug can cause nausea, vomiting.

Dose: 25–50 mg/kg.

5. **Lytic cocktail:** It is a mixture of chlorpromazine with meperidine and promethazine. Dose used is 0.5 mg/kg.

5. ANTIBIOTICS AND OTHER CHEMOTHERAPEUTICS

Q. 1. Write about the principle of antibiotic therapy.

(TNMGR, March 2010; BFUHS, May 2011)

Q. Discuss on selection of antimicrobial agent in orofacial infections.

(TNMGR, Sept. 2007)

Ans.

1. **Obtaining an accurate infectious disease diagnosis:** An infectious disease diagnosis is reached by determining the site of infection, defining the host, and establishing a microbiological diagnosis.
2. **Timing of initiation of antimicrobial therapy:** In critically ill patients, empiric therapy should be initiated immediately. In stable patients, antimicrobial therapy should be deliberately withheld until appropriate specimens have been collected.
3. **Empiric vs definitive antimicrobial therapy:** A common approach is to use broad-spectrum antimicrobial agents as initial empiric therapy. Once microbiology results are available, switch over to definitive therapy of narrow antibiotic spectrum.
4. **Interpretation of antimicrobial susceptibility tests:** Antimicrobial susceptibility testing measures the ability of a specific organism to grow in the presence of a particular drug *in vitro*. The goal is to predict the clinical success or failure of the antibiotic being tested against a particular organism.
5. **Bactericidal vs bacteriostatic therapy:** Bactericidal drugs, include drugs that primarily act on the cell wall (e.g. β -lactams), cell membrane (e.g. daptomycin), or bacterial DNA (e.g. fluoroquinolones). Bacteriostatic agents inhibit bacterial replication without killing the organism.
6. **Use of antimicrobial combinations:** Combination of 2 or more antimicrobial agents is recommended:
 - i. When agents exhibit synergistic activity against a microorganism.
 - ii. When critically ill patients require empiric therapy.
 - iii. To extend the antimicrobial spectrum beyond that achieved by use of a single agent for treatment of polymicrobial infections.
 - iv. To prevent emergence of resistance.

a. Host factors to be considered in selection of antimicrobial agents

1. *Renal and hepatic function:* If there is impairment of kidney and liver function, drugs dose need to be reduced.
2. *Age:* Most pediatric drug dosing is guided by weight. In geriatric patients, the serum creatinine level, the creatinine clearance should be estimated by factoring in age and weight for these patients.
3. *Genetic variation:* Genetic susceptibility to the adverse effects of antimicrobial agents is occasionally significant, before administration of certain drugs.
4. *Pregnancy and lactation:* Higher antimicrobial doses are not routinely recommended in the third trimester of pregnancy.
5. *History of allergy or intolerance.*
6. *History of recent antimicrobial use:* Eliciting a history of exposure to antimicrobial agents in the recent past (3 months) can also help in selection of antimicrobial therapy.
7. *Oral vs Intravenous therapy:* Patients hospitalized with infections are often treated with intravenous antimicrobial therapy. Patients with mild to moderate infections are treated with oral antimicrobial agents.

b. Pharmacodynamic characteristics: Along with host factors, the pharmacodynamic properties of antimicrobial agents may also be important in establishing a dosing regimen.

c. Efficacy at the site of infection: The efficacy of antimicrobial agents depends on their capacity to achieve a concentration equal to or greater than the minimum inhibitory concentration (MIC) at the site of infection and modification of activity at certain sites.

Considerations for continuing antibiotic therapy

1. *Duration of antimicrobial therapy:* It is important for clinicians to ensure that their patients fit the profile of the study population and carefully monitor high-risk patients for improvement.
2. *Assessment of response to treatment:* Response to treatment of an infection can be assessed using both clinical and microbiological parameters.
3. *Adverse effects:* A history of serious allergic reaction should be carefully documented to avoid inadvertent administration of the same drug or another drug in the same class.

Special situations in infectious disease therapy

1. *Antimicrobial therapy for foreign body associated infections:* As an alternative, for patients unable to tolerate implant removal, long-term suppressive antimicrobial therapy is sometimes used, with variable success.

2. *Use of antimicrobial agents as prophylactic or suppressive therapy:* For use of an antimicrobial agent as prophylactic treatment, the infection would occur predictably in a certain setting and would be well known to be associated with a specific organism or organisms, and an effective antimicrobial agent would be available with no or limited long-term toxicity.

Common misuses of antibiotics

1. Prolonged empiric antimicrobial treatment without clear evidence of infection.
2. Treatment of a positive clinical culture in the absence of disease.
3. Failure to narrow antimicrobial therapy when a causative organism is identified.
4. Prolonged prophylactic therapy.
5. Excessive use of certain antimicrobial agents.

Q. 2. Discuss the beneficial antimicrobial combinations and their clinical utility.

(TNMGR, Nov. 1995, April 1998)

Ans. The objectives of using antimicrobial combinations are:

1. *To achieve synergism:* Synergism may manifest in terms of decrease in the minimum inhibitory concentration (MIC) of antimicrobial agent (AMA). General guidelines are:
 - a. Two bacteriostatic agents are often additive, rarely synergistic.
 - b. Two bactericidal drugs are frequently additive and sometime synergistic if the organism is sensitive to both.
 - c. Combination of a bactericidal with a bacteriostatic drug may be synergistic or antagonistic depending on the organism. In general, if the organism is highly sensitive to the cidal drug-response to the combination is equal to the static drug given alone. If the organism has low sensitivity to the cidal drug-synergism may be seen.
2. *To reduce severity or incidence of adverse effects:* This is possible only if the combination is synergistic so that the doses can be reduced.
3. To prevent emergence of resistance.
4. To broaden the spectrum of antimicrobial action.

Disadvantages of antimicrobial combinations

1. They foster a casual rather than rational outlook in the diagnosis of infections and choice of AMA.
2. Increased incidence and variety of adverse effects.
3. Increased chances of super infections.

4. If inadequate doses of non-synergistic drugs are used—emergence of resistance may be promoted.
5. Increased cost of therapy.

Q. 3. Write a short note on uses of antibiotics in dentistry. (TNMGR, March 2007; MUHS, May 2009)

Ans. Indications

1. In patient where the host response is decreased by diseases like diabetes mellitus, malnutrition, etc.
2. Acute, severe rapidly spreading infections.
3. Pericoronitis, osteomyelitis, fracture, soft tissue infection, odontogenic infections.
4. As prophylactic measures for prevention of infections.
5. In postoperative wound infections.

Classification

a. According to their type of activity

- i. *Bactericidal agents*: Penicillins, cephalosporins, aminoglycoside, fluoroquinolones, rifampicin, metronidazole.
- ii. *Bacteriostatic agents*: Tetracyclines, chloramphenicol, sulphonamides, dapsone, macrolides.

b. According to spectrum of activity

- i. *Narrow spectrum*: Penicillins, aminoglycoside.
- ii. *Broad spectrum*: Tetracyclines, chloramphenicol.

c. According to mechanism of action

- i. *Inhibition of cell wall synthesis*: Penicillins, cephalosporins.
- ii. *Inhibition of cell membrane function*: Amphotericin B, nystatin.
- iii. *Inhibition of protein synthesis*: Tetracyclines, aminoglycoside, macrolides.
- iv. *Inhibition of DNA synthesis*: Acyclovir, ganciclovir.
- v. *Inhibition of DNA function*: Rifampicin, metronidazole.
- vi. *Inhibition of DNA gyrase*: Fluoroquinolones.
- vii. *Antimetabolite*: Sulphonamides, dapsone.

Q. 4. Discuss tetracyclines in detail. (MAHE, July 1999)

Ans. The tetracyclines used are tetracycline, demeclocycline, oxytetracycline, doxycycline, minocycline.

Mechanism of action: The tetracyclines are primarily bacteriostatic; inhibit protein synthesis by binding to 30S ribosomes in susceptible organism. Subsequent to such binding, attachment of aminoacyl t-RNA to the mRNA-ribosome complex is interfered. As a result, the peptide chain fails to grow.

Antimicrobial spectrum: All types of pathogenic microorganisms except fungi and viruses; hence the name 'broad-spectrum antibiotic'.

Resistance: In such bacteria, usually the tetracycline concentrating mechanism becomes less efficient or the

bacteria acquire capacity to pump it out. Another mechanism is plasmid mediated synthesis of a 'protection' protein which protects the ribosomal binding site from tetracycline. Elaboration of tetracycline inactivating enzymes is an unimportant mechanism of tetracycline resistance.

Pharmacokinetics: The older tetracyclines are incompletely absorbed from GIT; absorption is better if taken in empty stomach. Doxycycline and minocycline are completely absorbed irrespective of food. Tetracyclines are widely distributed in the body. Most tetracyclines are primarily excreted in urine by glomerular filtration; dose has to be reduced in renal failure; doxycycline is an exception to this. They are partly metabolized and significant amounts enter bile—some degree of enterohepatic circulation occurs.

Adverse effects

1. Epigastric pain.
2. Nausea.
3. Vomiting.
4. Diarrhea.
5. Esophageal ulceration.
6. Intramuscular injection of tetracyclines is very painful.
7. Thrombophlebitis.

Dose related toxicity

1. Liver damage.
2. Kidney damage.
3. Photo toxicity.
4. *Teeth and bones*: If given from midpregnancy to 5 months of extrauterine life, the deciduous teeth are affected: Brown discoloration, ill-formed teeth, more susceptible to caries. Tetracyclines given between 3 months and 6 years of age affect the crown of permanent anterior dentition.
5. Antianabolic effect.
6. Increased intracranial pressure.
7. Diabetes insipidus.
8. Vestibular toxicity.
9. Hypersensitivity.
10. Superinfection.

Precautions

1. Tetracyclines should not be used during pregnancy, lactation and in children.
2. They should be avoided in patients on diuretics: Blood urea may rise in such patients.
3. They should be used cautiously in renal or hepatic insufficiency.
4. Preparations should never be used beyond their expiry date.

5. Do not mix injectable tetracyclines with penicillin—inactivation occurs.
6. Do not inject tetracyclines intrathecally.

Uses

1. Empirical therapy.
2. Tetracyclines are the first choice drugs in:
 - a. *Venereal diseases*: Chlamydial nonspecific urethritis/endocervicitis, lymphogranuloma venereum, granuloma inguinale.
 - b. Atypical pneumonia.
 - c. Cholera.
 - d. Brucellosis.
 - e. Plague.
 - f. Relapsing fever.
 - g. Rickettsial infections.
3. *Tetracyclines are second choice drugs*
 - a. To penicillin/ampicillin for tetanus, anthrax, actinomycosis.
 - b. To ceftriaxone, amoxicillin or azithromycin for gonorrhea.
 - c. To ceftriaxone for syphilis in patients allergic to penicillin.
 - d. To penicillin for leptospirosis.
4. *Other situations in which tetracyclines may be used are*
 - a. Urinary tract infections.
 - b. Community-acquired pneumonia.
 - c. Amoebiasis.
 - d. Chronic obstructive lung disease.

Q. 5. Write a short note on newer penicillins.

(TNMGR, Oct. 1999)

Q. Write a short note on extended spectrum penicillins.

(TNMGR, March 2007)

Ans. Semisynthetic penicillins are produced by chemically combining specific side chains (in place of benzyl side chain of PnG) or by incorporating specific precursors. The aim of producing semisynthetic penicillins has been to overcome the shortcomings of PnG, which are:

1. Poor oral efficacy.
2. Susceptibility to penicillinase.
3. Narrow spectrum of activity.
4. Hypersensitivity reactions.

Classification

1. **Acid-resistant alternative to penicillin G**: Phenoxy-methyl penicillin (penicillin V).
2. **Penicillinase-resistant penicillins**: Methicillin, cloxacillin.

3. Extended spectrum penicillins

- a. *Aminopenicillins*: Ampicillin, bacampicillin, amoxicillin.
- b. *Carboxypenicillins*: Carbenicillin, ticarcillin.
- c. *Ureidopenicillins*: Piperacillin, mezlocillin.
4. *β -lactamase inhibitors*: Clavulanic acid, sulbactam, tazobactam.

1. Acid-resistant alternative to penicillin G

Phenoxymethyl penicillin (penicillin V): It is acid stable. Oral absorption is better. The antibacterial spectrum of penicillin V is identical to PnG.

Dose: 250–500 mg, infants 60 mg, children 125–250 mg; given 6 hourly (250 mg = 4 lac U).

2. **Penicillinase-resistant penicillins**: These congeners have side chains that protect the β -lactam ring from attack by staphylococcal penicillinase. These drugs are not resistant to gram-negative β -lactamases.

i. *Methicillin*: It is highly penicillinase resistant but not acid resistant, must be injected. Hematuria, albuminuria and reversible interstitial nephritis are the specific adverse effects of methicillin. It has been replaced by cloxacillin.

ii. *Cloxacillin*: It has an isoxazolyl side chain and is highly penicillinase as well as acid resistant. It is less active against PnG sensitive organisms.

Dose: 0.25–0.5 g orally every 6 hours; for severe infections 0.25–1 g may be injected IM or IV—higher blood levels are produced.

3. **Extended spectrum penicillins**: These semisynthetic penicillins are active against a variety of gram-negative bacilli as well. They can be grouped according to their spectrum of activity.

1. *Aminopenicillins*: This group has an aminosubstitution in the side chain. Some are prodrugs and all have quite similar antibacterial spectra. None is resistant to penicillinase or to other β -lactamases.

i. *Ampicillin*: It is active against all organisms sensitive to PnG; in addition, many gram-negative bacilli, e.g. *H. influenzae*, *E. coli*, *Proteus*, *Salmonella* and *Shigella* are inhibited. Ampicillin is not degraded by gastric acid; oral absorption is incomplete but adequate. Food interferes with absorption. It is partly excreted in bile and reabsorbed, entero-hepatic circulation occurs. However, primary channel of excretion is kidney, but tubular secretion is slower than for PnG; plasma $t_{1/2}$ is 1 hr.

Dose: 0.5–2 g oral/IM/IV depending on severity of infection, every 6 hours; children 25–50 mg/kg/day.

Uses

1. *Urinary tract infections*: Ampicillin has been the drug of choice.
2. Respiratory tract infections.
3. *Meningitis*: Ampicillin has been a first line drug, usually combined with a third generation cephalosporin/chloramphenicol for empirical therapy.
4. *Gonorrhea*: It is one of the first line drugs for oral treatment of nonpenicillinase producing gonococcal infections.
5. Typhoid fever.
6. Bacillary dysentery.
7. Cholecystitis: Ampicillin is a good drug because high concentrations are attained in bile.
8. Subacute bacterial endocarditis.
9. Septicemias and mixed infections.

Adverse effects

1. Diarrhea.
 2. Rashes.
 3. Hypersensitivity reactions.
- ii. *Bacampicillin*: It is an ester prodrug of ampicillin which is nearly completely absorbed from the GIT.; and is largely hydrolyzed during absorption. Thus, higher plasma levels are attained. Tissue penetration is also claimed to be better. Incidence of diarrhea is claimed to be lower.
Dose: 400–800 mg BD.
Talampicillin, pivampicillin, hetacillin are other prodrugs of ampicillin.
- iii. *Amoxicillin*: It is a close congener of ampicillin (but not a prodrug); similar to it in all respects except:
- Oral absorption is better; food does not interfere with absorption; higher and more sustained blood levels are produced.
 - Incidence of diarrhea is lower.
 - It is less active against *Shigella* and *H. influenzae*. Many physicians now prefer it over ampicillin for bronchitis, urinary infections, SABE and gonorrhea.
- Dose: 0.25–1 g TDS oral/IM
2. *Carboxypenicillins*
- i. *Carbenicillin*: The special feature of this penicillin congener is its activity against *Pseudomonas aeruginosa* and indole positive *Proteus* which are not inhibited by PnG or aminopenicillins. Carbenicillin is neither penicillinase-resistant nor acid resistant. It is inactive orally and is excreted rapidly in urine ($t_{1/2}$ is 1 hr). It is used as sodium

salt in a dose of 1–2 g IM or 1–5 g IV every 4–6 hours. High doses have also caused bleeding by interfering with platelet function.

- ii. *Ticarcillin*: It is more potent than carbenicillin against *Pseudomonas*, but other properties are similar to it.

3. *Ureidopenicillins*

- i. *Piperacillin*: This antipseudomonal penicillin is about 8 times more active than carbenicillin. It has good activity against *Klebsiella* and is used mainly in neutropenic/immunocompromised patients having serious gram-negative infections, and in burns. Elimination $t_{1/2}$ is 1 hr. Concurrent use of gentamicin or tobramycin is advised.

Dose: 100–150 mg/kg/day in 3 divided doses (max 16 g/day) IM or IV

- ii. *Mezlocillin*: It has activity similar to ticarcillin against *Pseudomonas* and inhibits *Klebsiella* as well. It is given parenterally primarily for infections caused by enteric bacilli.

Q. 6. Write a short note on infective endocarditis prophylaxis. (TNMGR, April 2000; RGUHS, Nov. 2011)

Q. Write a short note on antibiotic prophylaxis in cardiac patients. (TNMGR, Oct. 2000)

Q. Write a short note on antibiotic protocol in a patient of subacute bacterial endocarditis who needs a tooth extraction.

Ans. See table on next page

Q. 7. Write a short note on ciprofloxacin.

(TNMGR, Oct. 2000)

Ans. Ciprofloxacin is the most potent first generation fluoroquinolones (FQs) active against broad range of bacteria.

Highly susceptible organism: Aerobic gram-negative bacilli. For example, *E. coli*, *K. pneumoniae*, *Salmonella* sp., *Shigella*, *N. gonorrhoeae*, *H. influenzae*, etc.

Moderately susceptible: *Pseudomonas aeruginosa*, *Staph. aureus*, *Bacillus anthracis*, *M. tuberculosis*, etc.

The most prominent feature of ciprofloxacin is high tissue penetrability. Concentration in lung, sputum, muscle, bone, prostate and phagocytes exceeds than in plasma; CSF level are poor.

Mechanism of action: The FQs inhibit the enzyme bacterial DNA gyrase, which nicks double-stranded DNA, introduces negative super coils and then reseals the nicked ends. The DNA gyrase consists of two A and two B subunits: The A subunit carries out nicking of DNA, B subunit introduces negative super coils and

S. No.	Patient category	Oral medications	Non-oral medications*
1.	Adults, not allergic to penicillin	2.0 g Amoxicillin 1 h before procedure	2.0 g ampicillin IM or IV within 30 min before procedure
2.	Adults, penicillin allergic	600 mg clindamycin 1 h before procedure or 2.0 g cephalexin 1 hour before procedure OR 500 mg azithromycin or clarithromycin 1 h before procedure	600 mg clindamycin IV within 30 min before procedure OR 1.0 g cefazolin IM or IV within 30 min before procedure
3.	Children, not allergic to penicillin	50 mg/kg amoxicillin 1 h before procedure†	50 mg/kg ampicillin IM or IV within 30 min before procedure†
4.	Children, penicillin allergic	20 mg/kg clindamycin 1 h before procedure OR 50 mg/kg cephalexin or cefadroxil 1 h before procedure OR 15 mg/kg azithromycin or clarithromycin 1 h before procedure	20 mg/kg IV clindamycin within 30 min prior to procedure OR 25 mg/kg IM or IV cefazolin 30 min before procedure

IM: Intramuscularly; IV: Intravenously.

*For patients who are unable to take oral medications.

†The total pediatric dose calculated by weight should not exceed the adult dose.

then A subunit reseals the strands. FQs bind to A subunit with high affinity and interfere with its strand cutting and resealing function.

In **gram-positive bacteria** the major target of FQ action is a similar enzyme topoisomerase IV which nicks and separates daughter DNA strands after DNA replication. The bactericidal action probably results from digestion of DNA by exonucleases whose production is signaled by the damaged DNA.

In **mammalian cells** possess an enzyme topoisomerase II (that also removes positive super coils) which has very low affinity for FQs—hence the low toxicity to host cells.

Mechanism of resistance: Resistance is due to chromosomal mutation producing a DNA gyrase or topoisomerase IV with reduced affinity for FQs, or due to reduced permeability/increased efflux of these drugs across bacterial membranes.

The remarkable microbiological features of ciprofloxacin (also other FQs) are:

- Rapidly bactericidal activity and high potency.
- Relatively long post-antibiotic effect on Enterobacteriaceae, Pseudomonas and Staphylococcus.
- Low frequency of mutational resistance.
- Low propensity to select plasmid type resistant mutants.
- Protective intestinal streptococci and anaerobes are spared.
- Active against many β -lactam and aminoglycoside resistant bacteria.
- Less active at acidic pH.

Pharmacokinetics: Ciprofloxacin is rapidly absorbed orally, but food delays absorption, and first pass metabolism occurs. It is excreted primarily in urine; urinary and biliary concentrations are 10–50 folds higher than plasma.

Adverse effects

- **Gastrointestinal:** Nausea, vomiting, bad taste, anorexia.
- **CNS:** Dizziness, headache, restlessness, anxiety, insomnia, impairment of concentration and dexterity, tremor.
- **Skin/hypersensitivity:** Rash, pruritus, photosensitivity, urticaria, swelling of lips, etc.
- Tendonitis and tendon rupture.

Uses: Because of wide-spectrum bactericidal activity, oral efficacy and good tolerability, it is being extensively employed for blind therapy of any infection.

1. Urinary tract infections.
2. Gonorrhea.
3. Chancroid.
4. Bacteria gastroenteritis.
5. Typhoid.
6. Bone, soft tissue, gynecological and wound infections.
7. Respiratory infections.
8. Tuberculosis.
9. Meningitis.
10. Prophylaxis of infections in neutropenic/cancer patients.
11. Conjunctivitis.

Dose: Oral: 250–750 mg BD IV: 100–200 mg BD.

Q. 8. Write a short note on amoxicillin.

(TNMGR, April 2012)

Ans. Amoxicillin is type of semi-synthetic penicillins, produced by chemically combining specific side chains. It comes under the category of extended spectrum penicillins (aminopenicillins). This group has an amino substitution in the side chain. It is resistant to penicillinase or to other β -lactamases. It is active against all organisms sensitive to PnG; in addition, many gram-negative bacilli, e.g. *H. influenzae*, *E. coli*, *Proteus*, *Salmonella* and *Shigella* are inhibited. Penicillinase producing *Staph.* are not affected, as are other gram-negative bacilli, such as *Pseudomonas*, *Klebsiella*, indole positive *Proteus* and anaerobes like *Bacteroides fragilis*.

Pharmacokinetics: It is not degraded by gastric acid; oral absorption is incomplete but adequate. Food interferes with absorption. It is partly excreted in bile and reabsorbed-enterohepatic circulation occurs. However, primary channel of excretion is kidney; plasma $t_{1/2}$ is 1 hr.

Uses

1. **Urinary tract infections:** Drug of choice for most acute infections, but resistance has increased.
2. **Respiratory tract infections:** Bronchitis, sinusitis, otitis media, etc.
3. **Meningitis:** It is usually combined with a third generation cephalosporin/chloramphenicol for empirical therapy.
4. **Gonorrhea:** It is one of the first line drugs for oral treatment of nonpenicillinase producing gonococcal infections.
5. **Typhoid fever:** It is less efficacious than ciprofloxacin in eradicating carrier state.
6. Cholecystitis.
7. Subacute bacterial endocarditis.
8. Septicemias and mixed infections.

Oral absorption is better; food does not interfere with absorption; higher and more sustained blood levels are produced. Incidence of diarrhea is lower. It is less active against *Shigella* and *H. influenzae*.

Dose: 0.25–1 g TDS oral/IM

Adverse effects: Diarrhea (less frequent), rashes, allergy.

Q. 9. Write a short note on aminoglycoside.

(TNMGR, Oct. 2011)

Ans. These are a group of natural and semisynthetic antibiotics having polybasic amino groups linked

glycosidically to two or more amino sugar residues. All aminoglycosides are produced by soil actinomycetes and have many common properties.

a. Systemic aminoglycoside: Streptomycin, amikacin, gentamicin, sisomicin, kanamycin, netilmicin, tobramycin.

b. Topical aminoglycoside: Neomycin, framycetin.

Properties

1. All are used as sulfate salts, which are highly water soluble; solutions are stable for months.
2. They ionize in solution; are not absorbed orally; do not penetrate brain or CSF.
3. All are excreted unchanged in urine by glomerular filtration.
4. All are bactericidal and more active at alkaline pH.
5. They act by interfering with bacterial protein synthesis.
6. All are active primarily against aerobic gram-negative bacilli and do not inhibit anaerobes.
7. There is only partial cross resistance among them.
8. They have relatively narrow margin of safety.
9. All exhibit ototoxicity and nephrotoxicity.

Mechanism of action: They diffuse across the outer coat of gram-negative bacteria through porin channels. Inside the bacterial cell, streptomycin binds to 30S ribosome, but other aminoglycoside bind to additional sites on 50S subunit, as well as to 30–50S interface. They freeze initiation of protein synthesis, prevent polysome formation and promote their disaggregation to monosomes so that only one ribosome is attached to each strand of mRNA. The cidal action of these drugs appears to be based on secondary changes in the integrity of bacterial cell membrane.

Mechanism of resistance

- a. Acquisition of cell membrane bound inactivating enzymes.
- b. Mutation decreasing the affinity of ribosomal proteins that normally bind the aminoglycoside.
- c. Decreased efficiency of the aminoglycoside transporting mechanism.

Shared toxicities

1. **Ototoxicity:** The vestibular or the cochlear part may be primarily affected. Hearing loss affects the high frequency sound first. Headache is usually first to appear, followed by nausea, vomiting, dizziness, nystagmus, vertigo and ataxia.

2. **Nephrotoxicity:** It manifests as tubular damage resulting in loss of urinary concentrating power, low GFR, nitrogen retention, albuminuria and casts.
3. **Neuromuscular blockade:** All aminoglycosides reduce acetylcholine release from the motor nerve endings.

Precautions and interactions

1. **Avoid aminoglycoside during pregnancy:** Risk of fetal ototoxicity.
2. Avoid concurrent use of other ototoxic drugs, e.g. high ceiling diuretics, minocycline.
3. Avoid concurrent use of other nephrotoxic drugs, e.g. amphotericin B, vancomycin, cyclosporine and cisplatin.
4. Cautious use in patients past middle age and in those with kidney damage.
5. Cautious use of muscle relaxants in patients receiving an aminoglycoside.
6. Do not mix aminoglycoside with any drug in the same syringe/infusion bottle.

Q. 10. Describe the dosage of commonly used antibiotics prescribed for children.

(TNMGR, Sept. 2010)

Q. Write a short note on antibiotics used in pediatric dentistry.

(TNMGR, April 2013)

Ans. **Calculation of pediatric dose**

1. **Young's rule:**
Pediatric dose: $\text{Age} \times \text{adult dose} / \text{Age} + 12$
2. **Dilling's rule:**
Pediatric dose: $\text{Age} \times \text{adult dose} / 20$
3. **Clarke's rule:**
Pediatric dose: $\text{Weight (lb)} \times \text{adult dose} / 150$

Commonly used antibiotics

1. **Natural penicillins:** Penicillin G
Dose: Neonates: 50 mg/kg/day; infants and children: 100 mg/kg/day.
2. **Acid resistant penicillins:** Potassium phenoxymethyl penicillin.
Dose: 6–12 years: 250 mg; 1–5 years: 125 mg; <1 years: 62.5 mg, in four divided doses.
3. **Penicillase resistant penicillins:** Cloxacillin: 0.5–1 g/day in 3–4 divided doses.
4. **Extended spectrum penicillins:** Ampicillin: Children up to: 50–100 mg/kg/day. Amoxycillin: <12 years: 20–40 mg/kg/day TDS.
5. **Metronidazole:** 10–50 mg/kg/day TDS.
6. **Erythromycin:** 30–50 mg/kg/day QID.
7. **Clindamycin:** <1 month: 15–20 mg/kg/day, older children: 20–40 mg/kg/day.

8. **Tetracycline:** 20–40 mg/kg/day in divided doses.
9. **Nystatin:** <1 year: 100,000 units TDS, 1–6 years: 200,000 units TDS, >6 years: 500,000 units, TDS.

Q. 11. Write a short note on metronidazole.

(TNMGR, March 2008, Oct. 2012)

Ans. It is the prototype nitroimidazole, a highly active amoebicide. It has broad-spectrum cidal activity against protozoa, including *Giardia lamblia*. Many anaerobic bacteria, such as *Bact. fragilis*, *Fusobacterium*, *Clostridium perfringens*, *Cl. difficile*, *Helicobacter pylori*, *Campylobacter*, peptococci, spirochetes and anaerobic streptococci are sensitive. After entering the cell by diffusion its nitro group is reduced by certain redox proteins operative only in anaerobic microbes to highly reactive nitro radical which exerts cytotoxicity. The nitro radical of metronidazole acts as an electron sink which competes with the biological electron acceptors of the anaerobic organism for the electrons generated by the pyruvate: Ferredoxin oxidoreductase (PFOR) enzyme pathway of pyruvate oxidation. The energy metabolism of anaerobes is, thus, disrupted. Aerobic environment attenuates cytotoxicity of metronidazole by inhibiting its reductive activation.

Pharmacokinetics: Metronidazole is almost completely absorbed from the small intestines; a little unabsorbed drug reaches the colon. It is widely distributed in the body, attaining therapeutic concentration in vaginal secretion, semen, saliva and CSF. It is metabolized in liver primarily by oxidation and glucuronide conjugation, and excreted in urine. Plasma $t_{1/2}$ is 8 hrs.

Adverse effects: Anorexia, nausea, metallic taste and abdominal cramps.

Contraindications: Neurological disease, blood dyscrasias, first trimester of pregnancy and chronic alcoholism.

Interactions: A disulfiram-like intolerance to alcohol. Enzyme inducers may reduce its therapeutic effect. Cimetidine can reduce metronidazole metabolism. Metronidazole enhances warfarin action by inhibiting its metabolism.

Uses

1. **Amoebiasis:** Metronidazole is a first line drug for all forms of amoebic infection. For invasive dysentery and liver abscess: 800 mg TDS (children 30–50 mg/kg/day) for 7–10 days. For mild intestinal disease: 400 mg TDS for 5–7 days.
2. **Giardiasis:** It is highly effective in a dose of 400 mg TDS for 7 days.
3. **Trichomonas vaginitis:** It is the drug of choice; 400 mg TDS for 7 days.

4. Anaerobic bacterial infections.
5. *Pseudomembranous enterocolitis* due to *Cl. difficile* is generally associated with use of antibiotics. Oral metronidazole 800 mg TDS is more effective.
6. Ulcerative gingivitis, trench mouth 200–400 mg TDS (15–30 mg/kg/day).
7. Guinea worm infestation.

Q. 12. Write a short note on cephalosporins.

(TNMGR, Sept. 2008)

Ans. These are a group of semisynthetic antibiotics derived from 'cephalosporin-C' obtained from a fungus cephalosporium. The nucleus consists of a β -lactam ring fused to a dihydrothiazine ring (7-aminocephalosporanic acid). All cephalosporins are bactericidal and have the same mechanism of action as penicillin, i.e. inhibition of bacterial cell wall synthesis. However, they bind to different proteins than those which bind penicillins. This may explain differences in spectrum, potency and lack of cross resistance.

First generation cephalosporins: These were developed in the 1960s, have high activity against gram-positive but weaker against gram-negative bacteria.

Parenteral	Oral
Cephalothin	Cephalexin
Cefazolin	Cephadrine
Cefadroxil	

Second generation cephalosporins: These were developed subsequent to the first generation compounds and are more active against gram-negative organisms, with some members active against anaerobes, but none inhibits *P. aeruginosa*.

Parenteral	Oral
Cefuroxime	Cefaclor
Cefoxitin	Cefuroxime axetil

Third generation cephalosporins: These compounds introduced in the 1980s have highly augmented activity against gram-negative Enterobacteriaceae; some inhibit *Pseudomonas* as well. All are highly resistant to β -lactamases from gram-negative bacteria. However, they are less active on gram-positive cocci and anaerobes.

Parenteral	Oral
Cefotaxime	Cefixime
Ceftizoxime	Cefpodoxime proxetil
Ceftriaxone	Cefdinir
Ceftazidime	Ceftibuten
Cefoperazone	Ceftamet pivoxil

Fourth generation cephalosporins

Parenteral
Cefepime
Cefpirome

Adverse effects

1. Pain after injection.
2. Thrombophlebitis.
3. Diarrhea.
4. Hypersensitivity reactions.
5. Nephrotoxicity.
6. Bleeding.
7. Neutropenia and thrombocytopenia.
8. Disulfiram-like interaction with alcohol.

Uses

1. As alternatives to PnG; particularly in allergic patients.
2. Respiratory, urinary and soft tissue infections caused by gram-negative organisms.
3. Penicillinase producing staphylococcal infections.
4. Septicemias caused by gram-negative organisms.
5. Surgical prophylaxis.
6. Meningitis.
7. Gonorrhea.
8. Typhoid.
9. Mixed aerobic-anaerobic infections in cancer patients.
10. Hospital acquired infections.
11. Prophylaxis and treatment of infections in neutropenic patients.

Q. 13. Write a short note on antifungal agents.

(TNMGR, Oct. 2003; BFUHS, May 2011)

Ans.

Classification

1. Antibiotics

- a. *Polyenes*: Amphotericin B (AMB), nystatin, hamycin, natamycin (pimaricin).
- b. *Heterocyclic benzofuran*: Griseofulvin.

2. Antimetabolite: Flucytosine (5-FC).

3. Azoles

- a. *Imidazoles (topical)*: Clotrimazole, econazole, miconazole, oxiconazole (systemic): Ketoconazole
- b. *Triazoles (systemic)*: Fluconazole, itraconazole, voriconazole

4. Allylamine: Terbinafine

5. Other topical agents: Tolnaftate, undecylenic acid, benzoic acid, quiniodochlor, ciclopiroxolamine, butenafine, sod. thiosulfate.

Q. 12. Write a short note on antitubercular drugs.

(HP, May 2008)

Ans. First line drugs

1. Isoniazid (H)
2. Rifampin (R)
3. Pyrazinamide (Z)
4. Ethambutol (E)
5. Streptomycin (S)

Second line drugs: These drugs have either low anti-tubercular efficacy or high toxicity or both; are used in special circumstances only.

- | | |
|-----------------------------------|--------------------|
| 1. Thiacetazone (Tzn) | Newer drugs |
| 2. Para-aminosalicylic acid (PAS) | 1. Ciprofloxacin |
| 3. Ethionamide (Etm) | 2. Ofloxacin |
| 4. Cycloserine (Cys) | 3. Clarithromycin |
| 5. Kanamycin (Kmc) | 4. Azithromycin |
| 6. Amikacin (Am) | 5. Rifabutin |
| 7. Capreomycin (Cpr) | |

Q. 15. Write a short note on antisyphilitic drugs.

(BFUHS, May 2011)

Ans.

1. **Primary, secondary or early latent:** Penicillin G benzathine (single dose of 2.4 mU IM). If allergic to penicillin: Tetracycline hydrochloride (500 mg QID) or doxycycline (100 mg BID) for 2 weeks.
2. **Neurosyphilis:** Aqueous penicillin G (18–24 mU/day IV, given as 3–4 mU, every 4 hours for 10–14 days).
3. **Syphilis in pregnancy:** According to stage.

Q. 16. Write a short note on antiviral drugs.

(PAHER, May 2014)

Q. Write a short note on antiviral drugs used in HIV infection.

(RGUHS, September, 2007 and October, 2010)

Ans.**Classification**

1. **Anti-herpes virus:** Idoxuridine, acyclovir, valacyclovir, famciclovir, ganciclovir, foscarnet.
2. **Anti-retrovirus (for HIV)**
 - a. **Nucleoside reverse transcriptase inhibitors (NRTIs):** Zidovudine (AZT), didanosine, zalcitabine, stavudine, lamivudine, abacavir.
 - b. **Nonnucleoside reverse transcriptase inhibitors (NNRTIs):** Nevirapine, efavirenz, delavirdine.
 - c. **Protease inhibitors:** Ritonavir, indinavir, nelfinavir, saquinavir, amprenavir, lopinavir.

3. **Anti-influenza virus:** Amantadine, rimantadine.

4. **Nonselective antiviral drugs:** Ribavirin, lamivudine, adefovir dipivoxil, interferon α .

Q. 17. Write a short note on chemotherapy for oral cancer. (TNMGR, March 2007; BFUHS, Nov. 2003)**Ans. Types**

1. **Induction chemotherapy:** Given before other local therapies. Objective is to promote initial tumor reduction, and provide early treatment of micro-metastases.
2. **Concurrent chemotherapy:** Simultaneous with other therapy like radiotherapy is now the standard protocol treatment.
3. **Adjuvant chemotherapy:** It is given after the local therapy.

Agents used for the chemotherapy of oral cancer are

1. Methotrexate.
2. Bleomycin.
3. Taxol and derivatives.
4. Platinum derivatives (cisplatin, carboplatin).
5. 5-fluorouracil.
6. **Newer target directed agents:** EGFR, bevacizumab, erlotinib, capecitabine, interferon α -2b.

Q.18 Write a short note on anti-metabolites.

(TNMGR, Oct. 2013)

Ans.**Classification**

1. **Folate antagonist:** Methotrexate (Mtx).
2. **Purine antagonist:** 6-Mercaptopurine (6-MP), 6-thioguanine (6-TG), azathioprine, fludarabine.
3. **Pyrimidine antagonist:** 5-Fluorouracil (5-FU), cytarabine (cytosine arabinoside).

These are analogues related to normal components of DNA or of coenzymes involved in nucleic acid synthesis. They competitively inhibit utilization of the normal substrate or get themselves incorporated forming dysfunctional macromolecules.

1. Folate antagonist

Methotrexate (Mtx): It inhibits dihydrofolate reductase (DHFRase)—blocking the conversion of dihydrofolic acid (DHFA) to tetrahydrofolic acid (THFA) which is an essential coenzyme required for one carbon transfer reactions in purine synthesis and amino acid inter-conversions. It exerts major toxicity on bone marrow—low doses given repeatedly cause megaloblastic anemia, but high doses produce pancytopenia. Desquamation and bleeding may occur in GIT.

Methotrexate is absorbed orally, 50% plasma protein bound, a little metabolized and largely excreted unchanged in urine. The toxicity of Mtx cannot be overcome by folic acid, because it will not be converted to the active coenzyme form. However, folinic acid (N5 formyl THFA, cirtrovorum factor) rapidly reverses the effects.

Methotrexate is apparently curative in choriocarcinoma: 15–30 mg/day for 5 days orally or 20–40 mg/m² BSA IM or IV twice weekly.

It is highly effective in maintaining remission in children with acute leukemias, but not good for inducing remission: 2.5–15 mg/day. It is also useful in other malignancies, rheumatoid arthritis, psoriasis and as immunosuppressant.

2. Purine Antagonists

Mercaptopurine (6-MP) and thioguanine (6-TG): They are converted in the body to the corresponding mono-ribonucleotides which inhibit the conversion of inosine monophosphate to adenine and guanine nucleotides. They are especially useful in childhood acute leukemia, choriocarcinoma and have been employed in some solid tumors as well.

Azathioprine: It has marked effect on T-lymphocytes; suppresses cell mediated immunity (CMI) and is used primarily as immunosuppressant in organ transplantation, rheumatoid arthritis, etc. Azathioprine and 6-MP are metabolized by xanthine oxidase; their metabolisms are inhibited by allopurinol. Methylation by thiopurine methyl transferase (TPMT) is an additional pathway of 6-MP metabolism. Toxicity of azathioprine is also enhanced in TPMT deficiency.

The main toxic effect of antipurines is bone marrow depression. Mercaptopurine causes more nausea and vomiting than 6-TG. It also produces a high incidence of reversible jaundice. Hyperuricemia occurs with both. 6-Mercaptopurine: 2.5 mg/kg/day, half dose for maintenance.

3. Pyrimidine Antagonists

Pyrimidine analogues have varied applications as antineoplastic, antifungal and antipsoriatic agents.

Fluorouracil (5-FU): It is converted in the body to the corresponding nucleotide 5-fluoro-2-deoxyuridine monophosphate, which inhibits thymidylate synthase and blocks the conversion of deoxyuridilic acid to deoxythymidylic acid. Selective failure of DNA synthesis occurs due to non-availability of thymidylate. Fluorouracil itself gets incorporated into nucleic acids and this may contribute to its toxicity. Even resting cells are affected, though rapidly multiplying ones are more susceptible.

Dose: 1 g orally on alternate days (6 doses) then 1 g weekly or 12 mg/kg/day IV for 4 days to 6 mg/kg IV on alternate days.

It has been particularly used for many solid tumors—breast, colon, urinary bladder, liver, etc. Topical application in cutaneous basal cell carcinoma has yielded gratifying results.

Cytarabine: It is phosphorylated in the body to the corresponding nucleotide which inhibits DNA synthesis. It also interferes with DNA repair. Its main use is to induce remission in acute leukemia in children, also in adults. Other uses are: Hodgkin's disease and non-Hodgkin lymphoma.

Dose: 1.5–3 mg/kg IV BD for 5–10 days (also by continuous IV infusion).

Q. 19. Discuss the immunosuppressive drugs and their effects on oral tissue. (RGUHS, April, 2006)

Ans. Macrolides immunosuppressant

- i. **Agents:** Cyclosporine, tacrolimus, sirolimus.
- ii. **Effect on oral mucosa**
 1. Increased risk of infections.
 2. Cytochrome P450 system alteration.
 3. Gingival hyperplasia.
 4. May effect renal elimination of drugs.
 5. Risk of neoplasm.

a. Antimetabolite drugs

- i. **Agents:** Azathioprine, mycophenolate mofetil.
- ii. **Effect on oral mucosa**
 1. Increased risk of infections.
 2. Risk of neoplasm.

b. Polyclonal antibody

- i. **Agents:** Antithymocyte globulin, antilymphocyte globulin.
- ii. **Effect on oral mucosa:** Increased risk of infections.

c. Monoclonal antibody

- i. **Agents:** Muromonab-CD3, daclizumab, basiliximab.
- ii. **Effect on oral mucosa**
 1. Increased risk of infections.
 2. Risk of neoplasm.

d. Nonspecific immunosuppressant

- i. **Agents:** Corticosteroids.
- ii. **Effect on oral mucosa**
 1. Increased risk of infections.
 2. Poor wound healing.
 3. Risk of neoplasm.
 4. Steroid supplement needed during stressful procedure.

6. ANALGESICS AND ANTI-INFLAMMATORY

Q. 1. Classify NSAIDs. Explain therapeutically useful pharmacological actions of aspirin.

(TNMGR, April 2001, Sept. 2009)

Q. Write a short note on COX-2 inhibitors.

(TNMGR, March 2007; RGUHS, Oct. 2010)

Q. Classify anti-inflammatory drugs. Write a short note on the merits and demerits of each.(BFUHS, May 2009)

Q. Write a short note on NSAIDs used in dentistry.

(RGUHS, April, 2006; TNMGR, April 1995, Sept. 2008)

Q. Write about therapeutic uses of salicylates.

(KUHS, Jan., 2014)

Ans. Nonsteroidal anti-inflammatory drugs classification.

a. *Nonselective COX inhibitors (traditional NSAIDs)*

1. *Salicylates*: Aspirin.
2. *Propionic acid derivatives*: Ibuprofen, naproxen, ketoprofen, flurbiprofen.
3. *Anthranilic acid derivatives*: Mefenamic acid.
4. *Aryl-acetic acid derivatives*: Diclofenac, aceclofenac.
5. *Oxicam derivatives*: Piroxicam, tenoxicam.
6. *Pyrrolo-pyrrole derivative*: Ketorolac.
7. *Indole derivatives*: Indomethacin.
8. *Pyrazolone derivatives*: Phenylbutazone, oxyphenbutazone.

b. *Preferential COX-2 inhibitors*: Nimesulide, meloxicam, nebumetone.

c. *Selective COX-2 inhibitors*: Celecoxib, etoricoxib, parecoxib.

d. *Analgesics-antipyretics with poor anti-inflammatory action*:

1. *Paraaminophenol derivative*: Paracetamol (acetaminophen).
2. *Pyrazolone derivatives*: Metamizol (dipyrone), propiphenazone.
3. *Benzoxazocaine derivatives*: Nefopam.

Mechanism of action of NSAIDs: Prostaglandins (PGs), prostacyclin (PGI₂) and thromboxane A₂ (TXA₂) are produced from arachidonic acid by the enzyme cyclooxygenase, which exists in a constitutive (COX-1) and an inducible (COX-2) isoforms; the former serves physiological 'housekeeping' functions, while the latter, normally present in minute quantities, is induced by cytokines and other signal molecules at the site of inflammation → generation of PGs locally which mediate many of the inflammatory changes. Most

NSAIDs inhibit COX-1 and COX-2 nonselectively, but now some selective COX-2 inhibitors have been produced. Aspirin inhibits COX irreversibly by acetylating one of its serine residues; return of COX activity depends on synthesis of fresh enzyme. Beneficial actions due to PG synthesis inhibition

- Analgesia.
- Antipyresis.
- Anti-inflammatory.
- Antithrombotic.
- Closure of ductus arteriosus in newborn.

Other NSAIDs are competitive and reversible inhibitors of COX, return of activity depends on their dissociation from the enzyme, which in turn, is governed by the pharmacokinetic characteristics of the compound.

Analgesia: PGs induce hyperalgesia by affecting the transducing properties of free nerve endings—stimuli that normally do not elicit pain are able to do so. NSAIDs block the pain sensitizing mechanism induced by bradykinin, TNF- α , interleukins (ILs) and other algesic substances. They are, therefore, more effective against inflammation associated pain.

Antipyresis: NSAIDs reduce body temperature in fever, but do not cause hypothermia in normothermic individuals. Fever during infection is produced through the generation of pyrogens including, ILs, TNF- α , interferon's which induce PGE₂ production in hypothalamus—raise its temperature set point. NSAIDs block the action of pyrogens.

Shared toxicities due to PG synthesis inhibition

- Gastric mucosal damage.
- Bleeding: Inhibition of platelet function.
- Limitation of renal blood flow: Na⁺ and water retention.
- Delay/prolongation of labor.
- Asthma and anaphylactic reactions in susceptible individuals.

Anti-inflammatory: The most important mechanism of anti-inflammatory action of NSAIDs is considered to be inhibition of PG synthesis at the site of injury. The anti-inflammatory potency of different compounds roughly corresponds with their potency to inhibit COX. Certain NSAIDs may act by additional mechanisms including inhibition of expression/activity of some of these molecules and generation of superoxide/other free radicals. Stabilization of leukocyte lysosomal membrane and antagonism of certain actions of kinins may be contributing to NSAID action.

Dysmenorrhea: Level of PGs in menstrual flow, endometrial biopsy and that of $\text{PGF}_{2\alpha}$ metabolite in circulation are raised in dysmenorrheic women. NSAIDs lower uterine PG levels, afford excellent relief.

Antiplatelet: NSAIDs inhibit synthesis of both proaggregatory (TXA_2) and antiaggregatory (PGI_2) prostanoids, but effect on platelet TXA_2 (COX-1 generated) predominates \rightarrow therapeutic doses of most NSAIDs inhibit platelet aggregation-bleeding time is prolonged. Aspirin is highly active; acetylates platelet COX irreversibly in the portal circulation before it is deacetylated by first pass metabolism in liver. Small doses are therefore able to exert antithrombotic effect for several days.

Ductus arteriosus closure: During fetal circulation ductus arteriosus is kept patent by local elaboration of PGE_2 and PGI_2 . Unknown mechanisms switch off this synthesis at birth but when this fails to occur, small doses of indomethacin or aspirin bring about closure.

Parturition: Sudden spurt of PG synthesis by uterus probably triggers labor and facilitates its progression. Accordingly, NSAIDs have the potential to delay and retard labor.

Gastric mucosal damage: Gastric pain, mucosal erosion/ulceration and blood loss are produced by all NSAIDs to varying extents.

Renal effects: NSAIDs produce renal effects by at least 3 mechanisms:

- COX-1 dependent impairment of renal blood flow and reduction of GFR \rightarrow can worsen renal insufficiency.
- Juxtaglomerular COX-2 (probably COX-1 also) dependent Na^+ and water retention.
- Ability to cause papillary necrosis on habitual intake.

Anaphylactoid reactions: Aspirin precipitates asthma, angioneurotic swellings, urticaria or rhinitis in certain susceptible individuals.

Q. 2. Discuss the pharmacotherapy of orofacial pain.
(Nagpur Uni., 2002; RGUHS, April 2006)

Q. Discuss the drugs that control facial pain explaining the pharmacological reaction.

(TNMGR, March 2007)

Ans.

a. Nonsteroidal anti-inflammatory drugs

1. *Agents used:* Ibuprofen, naproxen, celecoxib, diflunisal, ketorolac, meloxicam.
2. *Indication:* Mild to moderate nociceptive pain, temporomandibular disorders.

b. Opiate analgesics

1. *Agents used:* Oxycodone, codeine sulfate, tramadol, fentanyl.
2. *Indications:* Moderate to severe nociceptive pain.

c. Adjuvant analgesics

1. *Agents used:* Carbamazepine, gabapentin, pregablin (anticonvulsants); amitriptyline, nortriptyline, imipramine (antidepressants); clonazepam, doxepin (anxiolytic); baclofen, cyclobenzaprine, tizanidine (muscle relaxants).
2. *Indications:* Cranial neuralgia, traumatic neuropathy, neuropathic pain of unknown reason, burning mouth, myofascial pain.

d. Topical analgesics

1. *Agents used:* Lidocaine, diphenhydramine, benzocaine, capsaicin.
2. *Indication:* Mucosal pain, superficial facial pain, stomatodynia.

Q.3. Write a short note on surface analgesics.

Ans. Surface or topical analgesics are mostly used as gels for application over painful muscles or joints.

Mechanism of action: The drug penetrates the subjacent tissue attaining high concentrations in the affected muscle/joints, while maintaining the low blood levels.

Indications

1. Osteoarthritis
2. Sprains
3. Backache
4. Spondylitis
5. Soft tissue rheumatism

Advantage

1. Less gastrointestinal and other systemic adverse effects.
2. Bypassing of first pass hepatic metabolism.

Disadvantage

1. Less efficacious.
2. Benefit is difficult to assess.

7. DENTAL PHARMACOLOGY

Q. 1. Write about uses of antiseptics in dentistry.

(TNMGR, March 2002)

Ans.

1. *As disinfectant of surgical instruments:* Formaldehyde, lysol, oxycyanide of mercury.
2. *As antiseptic wash and dressing:* Cetrimide (1%), gentian violet (2–5%), methylene blue (1–3%).

3. As *cleansing agent for wound*: Hydrogen peroxide (10–20%), potassium permanganate (0.5%).
4. As *preservative*: Phenol or cresol (0.5%), sodium metabisulphite (0.05–0.1%).
5. As *parasitocides*: Salicylic acid (2%).
6. *Insecticides*: Pyrethrum.

Q. 2. Write a short note on pharmacology of fluoride.

Q. Write a short note on fluorides in dental caries.

(TNMGR, March 2002)

Ans. The major route of fluoride absorption is through gastrointestinal tract. After absorption, fluoride is carried by blood and distributed to various tissues like teeth and bone; salivary glands; soft tissues. Fluoride level peaks 30 minutes after ingestion. The plasma half life is 4–10 hours. In plasma fluoride exists in two forms: Ionic and nonionic. About 99% of all fluorides in the human body are found in calcified tissues such as bone and teeth. 10–25% of the daily intake of fluoride is not absorbed and is excreted in feces. The elimination of absorbed fluoride occurs almost exclusively via the kidneys. The renal clearance of fluoride in the adult typically is 30–50 ml/min. Fluoride is also present in sweat, tears, breast milk, etc. Fluorides play an important role in reducing the susceptibility to dental caries.

Mechanism of action

1. Conversion of hydroxyapatite to fluoridated hydroxyapatite.
2. Increased rate of post-eruptive maturation.
3. Interference with microbial activity.
4. Alteration in plaque formation.
5. Alteration of tooth morphology.

Preparations: Fluoridated water, fluoride supplement, topical fluoride in the form of toothpaste, mouthwash, gel, varnish.

Q. 4. Write a short note on anti-plaque agents.

(TNMGR, March 2007; BFUHS, Nov. 2009)

Ans. Number of antimicrobial agents has been used to control the plaque:

1. **Bisbiguanide:** Chlorhexidine, alexidine and octenidine.
2. **Quaternary ammonium compounds:** Cetylpyridinium chloride (CPC) at concentration of 0.05%. The mechanism of action is related to their ability to rupture the cell wall and alter cytoplasmic contents.
3. **Povidone iodine (PVP-I):** Povidone-iodine is an iodophore and is microbicidal for gram +ve and

gram –ve bacteria, fungi, Mycobacterium, virus and protozoas.

4. **Salifluor:** Salifluor is a salicytonide (5n-octanoyl-3-trifluoromethylsalicylanide), with both antibacterial and anti-inflammatory property.
5. **Triclosan** (Trichloro-2-hydroxyl diphenyl ether): Triclosan is available in dentifrices and mouth rinses. Triclosan is both a bisphenol and a nonionic germicide with low toxicity. It has broad spectrum of antibacterial activity and lack the staining effects of cationic agents. Triclosan also act as an anti-inflammatory agent in mouth rinses.

6. Natural products

- a. **Sanguinarin chloride:** It is an alkaloid extract from blood root plant *Sanguinaria canadensis*.
- b. Propolis or naturally occurring bee product used by bees to seal opening on their hives at mainly consist of wax and plant extracts and contains flavones, flavanones and flavonols.

7. **Miscellaneous agents:** Salt of zinc and copper, enzymes (amylases, dextranase). Alcohol is an ingredient of most mouth rinses with plaque altering abilities.

Q. 5. Write a short note on chlorhexidine.

(TNMGR, April 2003)

Ans. Chlorhexidine is a bisbiguanide antiseptic. It is active against both gram-positive and gram-negative strains as well as fungi. It has bacteriostatic and bactericidal actions. It is a powerful, non-irritating cationic antiseptic that disrupts bacterial cell membrane, and denaturation of microbial proteins. It is relatively more active against gram-positive bacteria. It persists on the skin. The cationic nature of chlorhexidine minimizes absorption through the skin and mucosa, including from the gastrointestinal tract and it therefore displays very low toxicity.

Uses

1. As surgical scrub.
2. Neonatal bath.
3. In obstetrics.
4. General skin antiseptic.
5. In ocular infections (0.02%).
6. As an adjunct to oral hygiene and professional prophylaxis.
7. In recurrent oral ulceration.
8. Oral malodor.
9. In denture stomatitis patient.
10. As root canal disinfectant (2%).

Chlorhexidine is extensively used antiseptic in dentistry. Concentration used is 0.12–0.2% as mouthwash. 0.5–1% in toothpaste/gel. It is highly effective in preventing/treating gingivitis. In oral use as a mouth rinse, chlorhexidine has been reported to have a number of local side effects. These side effects are:

1. Brown discoloration of teeth.
2. Taste alteration.
3. Oral mucosa erosion.
4. Unilateral or bilateral parotid swelling.
5. Enhanced supragingival calculus formation.
6. Chlorhexidine also has a bitter taste which is difficult to mask completely.

Q. 6. Write a short note on disclosing agents.

(RGUHS, April 2007; HP, Aug. 2010)

Ans. Disclosing agents are preparations in liquid, tablet or lozenge, which contain dye or other coloring agents, which is used for the identification of bacterial plaque. Plaque can be distinctly seen providing a valuable visual aid and helps in the maintenance of oral hygiene.

1. **Erythrosine:** Most widely used; causes red staining of plaque.
2. **Fluorescent disclosing agent:** 0.75% sodium fluorescein solutions—plaque appears bright yellow in normal light, intensive yellow green under blue light. The disadvantage is requirement of special light source or filter mirror. This method is ideal who dislikes staining of teeth.
3. **Two-tone solution:** Multicoloring disclosing agent. Older plaque stains blue, newer plaque stains red.

Disclosing agents are available tablet/liquids. The tablet is chewed, swished and spit out. Liquid is applied with the help of cotton applicator.

Q. 7. Write uses of opioids in dentistry.

(TNMGR, Sept. 2002)

Ans. Moderate to severe pain can be managed by combination of NSAID with opioids. In acute pain, opioids are not recommended. They are routinely used for chronic, intractable pain. They act as mu receptor agonist and also mimic the effect of endogenous pain relieving chemicals. Various opioids used are oxycodone (5–30 mg), codeine sulfate (15–60 mg), hydromorphone (8 mg), meperidine (50–150 mg), tramadol (50–100 mg). Other uses are:

1. *As analgesics:* Opioids are indicated in severe pain of any type such as fracture of mandible.
2. *In preanesthetic medication:* To allay anxiety; to produce pre- and postoperative analgesia; to reduce the dose of anesthetic required.

3. In acute left ventricular failure.
4. As anxiolytic.
5. As anti-diarrheal.
6. *As antitussive agent:* Codeine and dextromethorphan are commonly used for dry cough.
7. *As a part of conscious sedation:* Fentanyl alone or with midazolam.

Q. 8. Write a short note on therapeutic uses of alcohol in dentistry.

(TNMGR, April 1998)

Ans.

1. As antiseptic: 70% ethanol.
2. Rubefacient and counter-irritant for sprains, joint pains, etc.
3. Rubbed into the skin to prevent bedsores.
4. Alcoholic sponges to reduce body temperature in fever.
5. Intractable neuralgias like trigeminal neuralgia and others: Injection of alcohol directly into the nerve trunks.
6. *Severe cancer pain:* Inj. of alcohol is used.
7. To ward off cold-may benefit by causing vasodilatation of blanched mucosa.
8. As appetite stimulant and carminative.
9. Reflex stimulation in fainting-1 drop in nose.
10. To treat methanol poisoning.

Q. 9. Discuss the drugs affecting orthodontic tooth movements.

(TNMGR, Oct. 2012)

Ans.

a. Analgesics

1. *NSAIDs like aspirin:* Slows the tooth movement.
2. *Selective NSAIDs:* No negative effect on tooth movement.
3. *Acetaminophen (paracetamol):* No effect on tooth movement.
4. *Indomethacin:* Slows the tooth movement.
5. *Flurbiprofen:* No significant effect on tooth movement.

b. Vitamin D: Enhances the rate of tooth movement.

c. Fluorides: Delay the tooth movement.

d. Bisphosphonates: Inhibit the tooth movement.

e. Hormones

1. *Estrogens:* Delay the tooth movement.
2. *Thyroid hormone:* Enhances the rate of tooth movement.
3. *Relaxin:* Enhances the rate of tooth movement.
4. *Calcitonin:* Inhibits the tooth movement.
5. *Parathyroid hormone:* Enhances the rate of tooth movement.

f. Corticosteroids: Enhances the rate of tooth movement.

- g. **Prostaglandins:** Low concentration enhances tooth movement; whereas high concentration leads to root resorption.
- h. **Interleukin antagonists:** Delay the tooth movement.
- i. **TNF- α antagonists:** Delay the tooth movement.
- j. **Immunomodulators:** Delay the tooth movement.
- k. **Immunosuppressants:** Delay the tooth movement.
- l. **Anticonvulsants:** Make the orthodontic treatment difficult because of gingival overgrowth.

Q. 10. Write a short note on sialogogue and anti-sialogogues. (TNMGR, March 2007; KUHS, Dec. 2012)

Ans.

a. Sialogogues

1. **Pilocarpine:** It is FDA approved sialogogue, especially after radiotherapy and in Sjögren's syndrome. It is a parasympathomimetic drug, acting as muscarinic agonist. *Dose:* 5–7.5 mg three to four times daily.
2. **Cevimeline:** It is a parasympathomimetic drug, acting as muscarinic agonist. *Dose:* 30 mg/three times daily.
3. **Bromhexine:** Mucolytic agent, stimulate the salivary as well as lacrimal secretions.
4. **Anetholetrithione:** Mucolytic agent, increases salivary secretion by upregulating the muscarinic receptors.

b. Anti-sialogogues

1. Scopolamine transdermal patch.
2. Glycopyrrolate: 1 mg every 4–6 hour
3. Atropine: 0.4 mg every 4–6 hour.
4. Diphenhydramine hydrochloride.
5. Amisulpride: 400 mg/day.

Q. 11. Write a short note on antioxidants.

(RGUHS, April 2007; Oct. 2010; TNMGR, Oct. 2011; Sumandeep Vidyapeeth, April 2011)

Ans. Antioxidants are compounds used by aerobic organisms for protection against oxidative stress, induced by free radicals and active oxygen species. They exert their protective action either by suppressing the formation of free radicals or by scavenging free radicals.

Antioxidants Classification

a. According to their location

1. **Plasma antioxidants:** β -carotene, ascorbic acid, bilirubin, uric acid, ceruloplasmin, transferrin.
2. **Cell membrane antioxidants:** α -tocopherol.
3. **Intracellular antioxidants:** Superoxide dismutase, catalase, glutathione peroxidase.

b. According to nature and action

1. **Non-enzymatic**

- a. **Nutrient antioxidants:** Carotenoid, α -tocopherol, ascorbic acid, selenium.
 - b. **Metabolic antioxidants:** Glutathione, ceruloplasmin, albumin, bilirubin, transferrin, ferritin, uric acid.
2. **Enzymatic:** Superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, glutathione transferase.

Antioxidants from diet play an important role in helping endogenous antioxidants for the neutralization of oxidative stress.

1. **Vitamin C:** It is essential for collagen, carnitine and neurotransmitters biosynthesis. Vitamin C works synergistically with vitamin E to quench free radicals and also regenerates the reduced form of vitamin E.
2. **Vitamin E:** Its antioxidant function mainly resides in the protection against lipid peroxidation. The dietary sources of vitamin E are vegetable oils, wheat germ oil, whole grains, nuts, cereals, fruits, eggs, poultry meat. Vitamin E has been proposed for the prevention against colon, prostate and breast cancers, some cardiovascular diseases, ischemia, cataract, arthritis and certain neurological disorders.
3. **Beta-carotene:** Beta-carotene is a fat soluble member of the carotenoid which is considered provitamins because it can be converted to active vitamin A. Beta-carotene is converted to retinol, which is essential for vision. It is a strong antioxidant and is the best quencher of singlet oxygen. Beta-carotene is present in many fruits, grains, oil and vegetables (carrots, green plants, squash, and spinach).
4. **Selenium:** Selenium is a trace element. It forms the active site of several antioxidant enzymes including glutathione peroxidase. Similar to selenium, the minerals manganese and zinc are trace elements that form an essential part of various antioxidant enzymes. Selenium is a trace mineral found in soil, water, vegetables (garlic, onion, grains, nuts, soybean), seafood, meat, liver, yeast.
5. **Lycopene:** Lycopene has been hypothesized to prevent carcinogenesis and atherogenesis by protecting critical cellular biomolecules, including lipids, lipoproteins, proteins, and DNA. Lycopene, when given in the dosage of 4.8 mg/day orally for 3 months leads to the reversal of dysplastic changes in leukoplakia and when given in the dosage of 16 mg/day leads to substantial increase in the mouth opening in oral submucous fibrosis. The major dietary source of lycopene is tomatoes with the lycopene in cooked tomatoes, tomato juice and tomato sauce included, being more bioavailable than that in raw tomatoes.

- 6. Flavonoids:** They are polyphenolic compounds which are present in most plants. The main natural sources of flavonoids include green tea, grapes (red wine), apple, cocoa (chocolate), ginkgo biloba, soybean, curcuma, berries, onion, and broccoli. They have been reported to prevent or delay a number of chronic and degenerative ailments such as cancer, cardiovascular diseases, arthritis, aging, cataract, memory loss, stroke, Alzheimer's disease, inflammation, infection. Green tea is a rich source of flavonoids, especially flavonols (catechins) and quercetin. Catechin levels are 4–6 times greater in green tea than in black tea. Many health benefits of green tea reside in its antioxidant, anticarcinogenic, anti-hypercholesterolemic, antibacterial (dental caries), anti-inflammatory activities.
- 7. Omega-3 and omega-6 fatty acids:** They are essential long-chain polyunsaturated fatty acids. Dietary sources of omega-6 fatty acids (linoleic acid) include vegetable oils, nuts, cereals, eggs, and poultry. It is important to maintain an appropriate balance of omega-3 and omega-6 in the diet, as these two substances work together to promote health.
- 8. Isoflavones:** These are found chiefly in soy products. Isoflavones are structural isomers of flavonoids and allocate biological properties with them. They have anti-estrogenic effects, and thus could act as chemopreventive agents in hormone dependent cancers.
- 9. Curcumin:** This is a plant phenol widely used as a spice (curry) and food-coloring agent. *In vivo* and *in vitro* studies have demonstrated that it may prevent initiation of DNA damage and is involved in anti-promotion mechanisms such as apoptosis. A number of animal studies have shown that curcumin is effective in inhibiting carcinogenesis in the skin, colon, stomach mammary gland and oral cavity.
- 10. Retinoids:** The best known retinoid is vitamin A or retinol, found in foods of animal origin, such as liver, milk and dairy products, egg yolk and fish liver oils, they are required for the maintenance of normal cell growth and differentiation. In contrast to carotenoid, they act primarily in the post-initiation phases of promotion and progression in carcinogenesis. Animal studies have shown that retinoid are potent to suppress or reverse epithelial carcinogenesis at several sites, especially oral carcinogenesis.
- 11. Vitamin D:** Major dietary sources of vitamin D include liver, fatty saltwater fish and eggs. Vitamin D inhibits proliferation and DNA synthesis, alters expression of several oncogenes, reduces lipid peroxidation and angiogenesis and induces differentiation. Epidemiologic studies support an inverse association among vitamin D intake and colorectal cancer risk.
- 12. Folic acid:** It is majorly found in fresh fruits and vegetables. Together with vitamin B₁₂, methionine and choline, it is involved in methyl group metabolism. A converse association involving dietary folate intake and adenomatous polyps or colorectal cancer has been stated in both case control and cohort studies.
- 13. Antioxidant-enzymes:** Superoxide dismutase, catalase, and glutathione peroxidase serve as primary line of defense in destroying free radicals.
- 14. Recent antioxidant:** Phloretin, tetracurcuminoid and ferulic acid, including formulations applied topically, can neutralize cell-damaging free radicals, particularly those caused by UV rays, nicotine, alcohol, and hydrogen peroxide. Certain antioxidants, including phloretin, silymarin, and hesperetin, significantly inhibit the inflammatory response associated with *Actinobacillus actinomycetemcomitans*. Lutein, dark green vegetables, Lignan, oatmeal, barley, rye, grape seed or pine bark extracts can also provide powerful antioxidant protection for the body.
- Mechanism of action of antioxidants:** Antioxidants neutralize free radicals by donating one of their electrons, which ends the electron stealing reaction. The antioxidant nutrient, however, does not become a free radical by donating an electron because they are stable in either form. Important antioxidants include the following:
1. Chain breaking or scavenging ones, such as vitamin E (alpha tocopherol), vitamin C (ascorbic acid), or vitamin A (beta carotene).
 2. Preventative antioxidants that function largely by sequestering transition metal ions and preventing Fenton reactions and are therefore largely proteins by nature (e.g. albumin, transferrin, or lactoferrin).
- Therapeutic use of antioxidants for oral lesions:** The possible uses of antioxidants for oral mucosal lesions include the following:
1. Prevention of lesions in high-risk individuals with mucosa that clinically appears normal with no history of either premalignant or malignant lesion.
 2. The treatment of premalignant oral lesions.
 3. In patients who have had either premalignant or malignant oral lesions that have been successfully treated, in order to prevent recurrence of the treated

initial lesion or to prevent the development of a second or a separate primary.

Q. 12. Drugs and gingival hyperplasia: List the drugs and their mechanism of action.

(TNMGR, October 2012)

Ans.

Anticonvulsants: Anticonvulsants causing gingival hyperplasia are phenytoin, sodium valproate, phenobarbitone, vigabatrin, primidone, mephenytoin, ethosuximide, methosuxinimide.

Immunosuppressant: Immunosuppressants causing gingival hyperplasia are cyclosporine, tacrolimus, sirolimus.

Calcium channel blockers: Calcium channel blockers causing gingival hyperplasia are nifedipine, nitrendipine, felodipine, nicardipine, manidipine, amlodipine, nimodipine, nisoldipine, verapamil, diltiazem.

Mechanism of action: The three major drugs causing gingival overgrowth, namely anticonvulsants, calcium channel blockers, and immunosuppressant; have similar mechanism of action at the cellular level.

1. All the drugs induce an increase in epithelial cell proliferation due to overexpression of antigen Ki67 and slight underexpression of the CDK-inhibitors p27^{KIP1} and p21^{WAF1}.
2. Disruption of homeostasis of collagen synthesis and degradation in gingival connective tissue, predominantly through the inhibition of collagen phagocytosis of gingival fibroblasts.
3. Existence of differential proportions of fibroblast subsets in each individual which exhibit a fibrogenic response to these medications.
4. Synergistic enhancement of collagenous protein synthesis by human gingival fibroblasts.
5. Negative effects on calcium ion influx across cell membranes, which interfere with the synthesis and function of collagenase.

Q. 13. Justify the importance of ozone therapy during management of pulp diseases. (BFUHS, May 2010)

Ans. Ozone is one of the most powerful antimicrobial agents available for use in dentistry.

Mechanism of Action

Effect on bacteria: Ozone acts on bacterial cell membranes, by oxidation of their lipid and lipoprotein components. Ozone seems to render the spores defective in germination, perhaps because of damage to the spore's inner membrane.

Effect on virus: All viruses are susceptible to ozone; yet differ widely in their susceptibility. Lipid-enveloped viruses are especially sensitive to ozone, ozone causes damage to polypeptide chains and envelope proteins impairing viral attachment capability, and breakage of viral RNA.

Effect on fungal and protozoa: Ozone inhibits cell growth at certain stages.

Effect on blood cells: Ozone reduces or eliminates clumping of red blood cells and its flexibility is restored, along with oxygen carrying ability. There is a stimulation of the production of glutathione peroxidase, catalase, and superoxide dismutase which act as free radical scavengers.

Effect on leukocytes: Ozone behaves as a weak cytokine such as tumor necrosis factor- α (TNF- α), interleukin-2, interleukin-6, interleukin-8, transforming growth factor- β (TGF- β) inducer. Ozone reacts with the unsaturated fatty acids of the lipid layer in cellular membranes, forming hydrogen peroxides (H₂O₂), one of the most significant cytokine inducers.

Platelets: H₂O₂ generated by blood ozonation activate phospholipase C, phospholipase A₂, cyclo-oxygenases and lipo-oxygenases, and thromboxane synthetase, allowing a step increase of intracellular calcium, release of prostaglandin E₂, prostaglandin F_{2 α} , and thromboxane A₂ with irreversible platelet aggregation.

Modes of ozone administration

- Ozone gas application with a silicone cup.
- Ozone aqueous solution.
- Ozone oil.

Advantages of topical ozone therapy

1. There is no chance of development of resistance oxidative challenges of ozone.
2. In addition, there is evidence that ozone directly inactivates bacterial toxins.

Uses in endodontics: The oxidative power of ozone characterizes it as an efficient antimicrobial. Its antimicrobial action has been demonstrated against bacterial strains, such as *Micobacteria*, *Streptococcus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Peptostreptococcus*, *Enterococcus faecalis*, and *Candida albicans*. *In vitro* studies showed that ozone was effective over most of the bacteria found in cases of pulp necrosis. Ozone works best when there is less organic debris remaining. Therefore, the recommendation is to use either ozonated water or ozone gas at the end of the cleaning and shaping process. Ozone is effective

when it is used in sufficient concentration, for an adequate time. Ozone will not be effective if too little dose of ozone is delivered or it is not delivered appropriately.

Ozone therapy and dental caries: Ozone therapy is used as an atraumatic treatment modality in dental practice. In small, non-cavitated lesions showed a greater reduction in number of microorganisms after the application of ozone than did larger lesions, and lesions closer to the gingival margin also showed less reduction in the number of microorganisms. Non-cavitated lesions are more likely to reverse than cavitated lesions. It has been shown that the infusion of ozone into noncarious dentine prevented biofilm formation *in vitro* from *S. mutans* and *L. acidophilus* over a 4-week period. The longer the contact time, the better the microbiological kill rate.

Ozone had no influence on the physical properties of the enamel to enhance or hinder the sealing ability. Thus, ozone can be applied over intact and prepared enamel during the restoration process. The application of ozone on dentin could be performed by the dental clinician without impairing the micromechanical properties of the substrate.

8. HEMATINICS, COAGULANTS AND ANTICOAGULANTS

Q. 1. Discuss coagulants.

(Sumandeep Vidyapeeth, April 2011;
TNMGR, April 2012)

Q. Mention the role of vitamin K in clotting mechanism.

(TNMGR, March 2007)

Ans. These are substances which promote coagulation and are indicated in hemorrhagic states. Fresh whole blood or plasma provide all the factors needed for coagulation and are the best therapy for deficiency of any clotting factor; also they act immediately. Other drugs used to restore hemostasis are:

1. Vitamin K

K_1 (from plants, fat soluble): Phytonadione (phylloquinone).

K_3 (synthetic)

- **Fat-soluble:** Menadione, acetomenaphthone.
- **Water-soluble:** Menadione sod. bisulfite, menadione sod. diphosphate.

2. Miscellaneous

- Fibrinogen (human).
- Antihemophilic factor.
- Desmopressin.
- Adrenochrome monosemicarbazone.
- Rutin, ethamsylate.

a. Vitamin K: It is a fat-soluble dietary principle required for the synthesis of clotting factors.

Dietary sources: Green leafy vegetables, such as cabbage, spinach; and liver, cheese, etc.

Daily requirement: 50–100 µg/day.

Action: Vit K acts as a cofactor at a late stage in the synthesis by liver of coagulation proteins—prothrombin, factors VII, IX and X.

Utilization: Fat-soluble—absorbed from the intestine via lymph. Water-soluble forms—absorbed directly into portal blood. It is metabolized in liver; metabolites are excreted in bile and urine.

Deficiency: Due to liver disease, obstructive jaundice, malabsorption, long-term antimicrobial therapy. The most important manifestation is bleeding tendency; Hematuria is usually first to occur; other common sites of bleeding are GIT, nose and under the skin ecchymoses.

Use: The only use of vit K is in prophylaxis and treatment of bleeding due to deficiency of clotting factors in the following situations:

- Dietary deficiency of vit K.
- Prolonged antimicrobial therapy.
- Obstructive jaundice or malabsorption syndromes.
- Liver disease (cirrhosis, viral hepatitis).
- Newborns.
- Overdose of oral anticoagulants.
- Prolonged high dose salicylate therapy causes hypoprothrombinemia.

Toxicity: Rapid IV injection of emulsified vit K produces flushing, breathlessness; constriction in the chest, fall in BP. Menadione and its water-soluble derivatives can cause hemolysis in a dose-dependent manner. In the newborn menadione or its salts can precipitate kernicterus.

b. Fibrinogen: To control bleeding in hemophilia, antihemophilic globulin (AHG) deficiency and acute afibrinogenemic states; 0.5 g is infused IV.

c. Antihemophilic factor: It is indicated (along with human fibrinogen) in hemophilia and AHG deficiency. Dose: 5–10 U/kg by IV infusion, repeated 6–12 hourly.

d. Desmopressin: It releases factor VIII and von Willebrand's factor from vascular endothelium and checks bleeding in hemophilia and von Willebrand's disease.

e. Adrenochrome monosemicarbazone: It is believed to reduce capillary fragility, control oozing from raw

surfaces and prevent micro-vessel bleeding, e.g. epistaxis, hematuria, retinal hemorrhage, secondary hemorrhage from wounds, etc. Dose: 1–5 mg oral, IM.

f. Rutin: It is a plant glycoside claimed to reduce capillary bleeding. It has been used in a dose of 60 mg oral BD-TDS along with vit C which is believed to facilitate its action.

g. Ethamsylate: It reduces capillary bleeding when platelets are adequate; probably exerts anti-hyaluronidase action—improves capillary wall stability, but does not stabilize fibrin (not an antifibrinolytic). Ethamsylate has been used in the prevention and treatment of capillary bleeding in menorrhagia, after abortion, epistaxis, malena, and hematuria and after tooth extraction, but efficacy is unsubstantiated. Side effects are nausea, rash, headache, and fall in BP (only after IV injection). Dose: 250–500 mg TDS oral/IV.

Q. 2. Write a short note on hemostatic/styptics.

(TNMGR, April 1995)

Ans. They are the substances used to stop bleeding from a local and approachable site. They are particularly effective on oozing surfaces, e.g. tooth socket, abrasions, etc. Absorbable materials like **fibrin, gelatin foam, and oxidized cellulose** provide a meshwork which activates the clotting mechanism and checks bleeding. Left *in situ* these materials are absorbed in 1–4 weeks and generally cause no foreign body reaction. **Thrombin** obtained from bovine plasma may be applied as dry powder or freshly prepared solution to the bleeding surface in hemophiliacs. Vasoconstrictors like 0.1% **Adr** solution may be soaked in sterile cotton-gauze and packed in the bleeding tooth socket or nose in case of epistaxis to check bleeding when spontaneous vasoconstriction is inadequate. Astringents such as **tannic acid or metallic salts** are occasionally applied for bleeding gums, bleeding piles, etc.

Q. 3. Write a short note on sclerosing agents.

Ans. These are irritants, cause inflammation, coagulation and ultimately fibrosis, when injected into hemorrhoids (piles) or varicose vein mass. They are used only for local injection.

1. *Phenol (5%) in almond oil or peanut oil:* 2–5 ml.
2. *Ethanolamine oleate (5% in 25% glycerine and 2% benzyl alcohol):* 1–5 ml inj.
3. *Sod. tetradecyl sulfate (3% with benzyl alcohol 2%):* 0.5–2 ml at each site.
4. *Polidocanol (3% inj):* 2 ml.

Q. 4. Write a short note on thrombolytic/anti-coagulants drugs.

(TNMGR, March 2002, 2012; KLE Uni. Dec.2008)

Ans. These are drugs used to lyse thrombi/clot to recanalize occluded blood vessels (mainly coronary artery). They are curative rather than prophylactic; work by activating the natural fibrinolytic system.

The clinically important fibrinolytic are

1. **Streptokinase (Stk):** It is obtained from β -hemolytic Streptococci group C. It is inactive as such, combines with circulating plasminogen to form an activator complex which then causes limited proteolysis of other plasminogen molecules to plasmin. Its $t_{1/2}$ is estimated to be 30–80 min. Streptokinase is antigenic; can cause hypersensitivity reactions and anaphylaxis. Fever is common, hypotension and arrhythmias are reported.
2. **Urokinase:** It is an enzyme isolated from human urine; now prepared from cultured human kidney cells, which activates plasminogen directly and has a plasma $t_{1/2}$ of 10–15 min. It is non-antigenic. Fever occurs during treatment, but hypotension and allergic phenomena are rare. Indicated in patients in whom streptokinase has been used for an earlier episode.
3. **Alteplase (recombinant tissue plasminogen activator (rt-PA):** Produced by recombinant DNA technology from human tissue culture, it specifically activates gel phase plasminogen already bound to fibrin, and has a little action on circulating plasminogen. It is rapidly cleared by liver and has a plasma $t_{1/2}$ of 4–8 min. Because of the short $t_{1/2}$, it needs to be given by slow IV infusion and often requires heparin co-administration. It is non-antigenic, but nausea, mild hypotension and fever may occur. It is expensive.
4. **Tenecteplase:** It is a mutant variant of rt-PA with higher fibrin selectivity and longer duration of action. A single IV bolus dose (0.5 mg/kg) or split into two doses 30 min apart is given. The clinical efficacy and risk of bleeding with reteplase and tenecteplase are similar to alteplase.

Uses of fibrinolytic

1. Acute myocardial infarction.
2. Deep vein thrombosis.
3. Pulmonary embolism.
4. Peripheral arterial occlusion.
5. Stroke.

Q. 5. Write about oral and parenteral iron preparations, their indications and toxicity.

(TNMGR, Oct. 1999, April 2012)

Ans.

1. Oral iron preparations

- Ferrous sulfate* (hydrated salt 20% iron, dried salt 32% iron): Cheapest, causes metallic taste in mouth, e.g. tablet Fersolate (200 mg).
- Ferrous gluconate* (12% iron): For example, tab. Ferricum (400 mg). Elixer (400 mg/15 ml).
- Ferrous fumarate* (33% iron): Less water-soluble, tasteless. Tab. Nori-A (200 mg).
- Colloidal ferric hydroxide* (50% iron): For example, tab. Neoferum (200 mg).
- Ferrous succinate (35% iron).
- Iron choline citrate.
- Iron calcium complex (5% iron).
- Ferric ammonium citrate (scale iron).
- Ferrous aminoate (10% iron).
- Ferric glycerophosphate.
- Iron hydroxyl polymaltose.

2. Parenteral iron preparation

- Iron-dextran*: 50 mg elemental iron/ml, e.g. Imferon (2 ml).
- Iron-sorbitol*: Citric acid complex: 50 mg elemental iron/ml. For example, Jectofer (1.5 ml).

Uses

- Iron deficiency anemia**: It is the most important indication for medicinal iron. A rise in Hb level by 0.5–1 g/dl per week is an optimum response to iron therapy. It is faster in the beginning and when anemia is severe.
- Megaloblastic anemia**: When brisk hemopoiesis is induced by vit B₁₂ or folate therapy, iron deficiency may be unmasked.
- As an astringent**: Ferric chloride is used in throat paint.

Toxicity

Adverse effects of oral iron: Epigastric pain, heartburn, nausea, vomiting, staining of teeth, metallic taste, bloating, colic. Constipation is more common than diarrhea.

Adverse effects of parenteral iron: Local pain at site of IM injection, pigmentation of skin, sterile abscess, fever, headache, joint pains, flushing, palpitation, chest pain, dyspnea, lymph node enlargement. A metallic taste in mouth lasting a few hours occurs with iron-sorbitol injection.

9. ANTI-DIABETICS AND OTHER HORMONES**Q. 1. Write a short note on antidiabetic drugs.**

(TNMGR, March 2011; BFUHS, Oct. 2011)

Q. Write a note on oral sulphonylurease.

(TNMGR, Nov. 2001, March 2007)

Ans.

Classification of Antidiabetic Drugs**1. Sulphonylureas**

- First generation*: Tolbutamide, chlorpropamide.
- Second generation*: Glibenclamide, glipizide, gliclazide, glimepiride.

2. Biguanide: Metformin.**3. Meglitinide analogue**: Repaglinide.**4. D-phenylalanine derivative**: Nateglinide.**5. Thiazolidinediones**: Rosiglitazone, pioglitazone.**6. α -glucosidase inhibitor**: Acarbose.

Mechanism of action of sulphonylureas: Sulphonylureas act on the so-called 'sulphonylurea receptors' (SUR1) on the pancreatic β cell membrane—cause depolarization by reducing conductance of ATP sensitive K⁺ channels. This enhances Ca²⁺ influx \rightarrow degranulation. The rate of insulin secretion at any glucose concentration is increased. The sulphonylureas primarily augment the 2nd phase insulin secretion with a little effect on the 1st phase.

Pharmacokinetics: All sulphonylureas are well absorbed orally, and are 90% or more bound to plasma proteins. Some are primarily metabolized—may produce active metabolite; others are mainly excreted unchanged in urine.

Interactions: Drugs that enhance sulphonylurea action are:

- Displace from protein binding*: Phenylbutazone, sulfinpyrazone, salicylates, sulfonamides, PAS.
- Inhibit metabolism/excretion*: Cimetidine, sulfonamides, warfarin, chloramphenicol, and acute alcohol intake.
- Synergize with or prolong pharmacodynamic action*: Salicylates, propranolol, sympatholytic antihypertensive, lithium, theophylline, alcohol.

Drugs that decrease sulphonylurea action are

- Induce metabolism*: Phenobarbitone, phenytoin, rifampicin, chronic alcoholism.
- Opposite action/suppress insulin release*: Corticosteroids, thiazides, furosemide, oral contraceptives.

Adverse effects

- Hypoglycemia**.
- Nonspecific side effects**: Nausea, vomiting, flatulence, diarrhea or constipation, headache, paresthesias and weight gain.
- Hypersensitivity**: Rashes, photosensitivity, purpura, transient leukopenia, agranulocytosis.

Q. 2. Write a short note on types of insulin.

(TNMGR, Oct. 2011)

Ans.**a. Based on source**

1. Bovine insulin.
2. Porcine insulin.
3. Human insulin.

b. Based on purity

1. Single peak insulin.
2. Monocomponent insulin.

c. Based on onset and duration of action

1. *Ultra-short acting insulin*: Insulin lispro, insulin aspart.
2. *Short acting insulin*: Regular soluble insulin.
3. *Intermediate acting insulin*: NPH, lente.
4. *Long acting insulin*: Ultralente, protamine zinc insulin.

Q. 3. Write a short note on calcitonin.

(TNMGR, Nov. 2001)

Ans. Calcitonin is the hypocalcemic hormone produced by parafollicular 'C' cells of thyroid. Parathyroid, thymus and cells of medullary carcinoma of thyroid also contain calcitonin. Synthesis and secretion of calcitonin is regulated by plasma Ca^{2+} concentration itself: Rise in plasma Ca^{2+} increases, while fall in plasma Ca^{2+} decreases calcitonin release. The plasma $t_{1/2}$ of calcitonin is 10 min, but its action lasts for several hours.

Actions: The actions of calcitonin are generally opposite to that of parathyroid hormone (PTH). It inhibits bone resorption by direct action on osteoclasts—decreasing their ruffled surface which forms contact with the resorptive pit. Calcitonin inhibits proximal tubular calcium and phosphate reabsorption by direct action on kidney. However, hypocalcemia overrides the direct action by decreasing the total calcium filtered at the glomerulus—urinary Ca^{2+} is actually reduced.

Preparation and units: Synthetic salmon calcitonin is used clinically, because it is more potent due to slower metabolism. Human calcitonin has also been produced. 1 IU = 4 µg of standard preparation.

Adverse effects: Nausea, flushing, tingling of fingers, bad taste and allergic reaction.

Uses

1. *Hypercalcemic states*: Hyperparathyroidism, hypervitaminosis D, osteolytic bony metastasis and hypercalcemia of malignancy; 4–8 IU/kg IM 6–12 hourly only for 2 days.

2. *Postmenopausal osteoporosis*: 100 IU s.c. or IM daily along with calcium and vit D supplements.

3. *Paget's disease*: 100 U daily or on alternate days produces improvement for a few months.

Q. 3. Write a short note on pharmacology of drugs which affects calcium homeostasis.

(TNMGR, Nov. 1995, March 2008)

Ans. Calcium constitutes about 2% of body weight. Over 99% of this is stored in bones, the rest being distributed in plasma and all tissues and cells.

Physiological Roles

1. Calcium controls excitability of nerves and muscles.
2. Regulates permeability of cell membranes. It also maintains integrity of cell membranes and regulates cell adhesion.
3. Ca^{2+} ions are essential for excitation-contraction coupling in all types of muscle and excitation-secretion coupling in exocrine and endocrine glands, release of transmitters from nerve ending and other release reactions.
4. Intracellular messenger for hormones, autacoids and transmitters.
5. Impulse generation in heart—determines level of automaticity and AV conduction.
6. Coagulation of blood.
7. Structural function in bone and teeth.

Plasma calcium level precisely regulated by 3 hormones, viz. parathormone (PTH), calcitonin and calcitriol (active form of vit D). These regulators control its intestinal absorption, exchange with bone and renal excretion. In addition, several other hormones, metabolites and drugs influence calcium homeostasis.

a. Influences affecting bone turnover → ↑ bone → resorption → increase in serum calcium level

- Corticosteroids.
- Parathormone.
- Thyroxine (excess).
- Hypervitaminosis D.
- Prostaglandin E_2
- Interleukin 1 and 6.
- Alcoholism.
- Loop diuretics.

b. Influences affecting bone turnover → ↓ bone resorption → decrease in serum calcium level

- Androgens/estrogens.
- Calcitonin.
- Growth hormone.
- Bisphosphonates.
- Fluoride.

- Gallium nitrate.
- Mithramycin.
- Thiazide diuretics.

Normal plasma calcium is 9–11 mg/dl. (40% is bound to plasma proteins; 10% is complexed with citrate, phosphate and carbonate in an undissociable form; the remaining (about 50%) is ionized and physiologically important).

Preparations

1. **Calcium chloride (27% Ca):** Freely water-soluble but highly irritating—tissue necrosis occurs if it is injected IM or extravasation takes place during IV injection. Orally also the solution irritates.
2. **Calcium gluconate (9% Ca):** It is non-irritating to GIT. and the vascular endothelium—a sense of warmth is produced on IV injection: Extravasation should be guarded. It is the preferred injectable salt.
3. **Calcium lactate (13% Ca):** Given orally, nonirritating and well tolerated.
4. **Calcium dibasic phosphate (23% Ca):** Insoluble reacts with HCl to form soluble chloride in the stomach. It is bland; used orally as antacid and to supplement calcium.
5. **Calcium carbonate (40% Ca):** Insoluble, tasteless and nonirritating. It has been used as antacid—reacts with HCl to form chloride which may be absorbed from the intestines.

Side effects: Constipation, bloating and excess gas.

Use

1. **Tetany:** 10–20 ml of calcium gluconate (elemental calcium 90–180 mg) IV over 10 min, followed by slow IV infusion.
2. **As dietary supplement:** In growing children, pregnant, lactating and menopausal women. The dietary allowance recommended by National Institute of Health (1994) is
 - Children (1–10 yr): 0.8–1.2 g
 - Young adult (11–24 yr), pregnant and lactating women: 1.2–1.5 g
 - Men (25–65 yr), women (25–50 yr) and (51–65) yr if taking HRT: 1.0 g
 - Women (51–65 yr) not taking HRT, every one > 65 yr: 1.5 g
3. **Osteoporosis:** In the prevention and treatment of osteoporosis with HRT/raloxifene/alendronate.
4. **Empirically,** calcium gluconate IV has been used in dermatoses, paresthesias, weakness and other vague complaints.
5. **As antacid.**

Parathyroid hormone (PTH): PTH increases plasma calcium levels by:

1. **Bone:** PTH promptly increases resorption of calcium from bone. This is the most prominent action of PTH.
2. **Kidney:** PTH increases calcium reabsorption in the distal tubule. It also promotes phosphate excretion which tends to supplement the hypercalcemic effect.
3. **Intestines:** PTH has no direct effect on calcium absorption but increases it indirectly by enhancing the formation of calcitriol (active form of vit D) in the kidney by activating 1α -hydroxylase. Calcitriol then promotes intestinal absorption of calcium.

Calcitonin

1. The actions of calcitonin are generally opposite to that of PTH. It inhibits bone resorption by direct action on osteoclasts—decreasing their ruffled surface which forms contact with the resorptive pit.
2. Calcitriol enhances resorption of calcium and phosphate from bone by promoting recruitment and differentiation of osteoclast precursors in the bone remodeling units.
3. Calcitriol enhances tubular reabsorption of calcium and phosphate in the kidney.

10. CORTICOSTEROIDS

Q. 1. Describe the regulatory mechanism of steroid secretions. Enlist the pharmacological actions of steroids. Discuss the role of corticosteroids in treatment of oral pathologies.

(MUHS, May 2010; RGUHS, May 2011)

Q. Write about indications for corticosteroid therapy.
(TNMGR, Oct. 1999)

Ans.

Regulatory mechanism: Synthesis and release of glucocorticoids is controlled by pituitary ACTH, which is stimulated in turn by CRF, which is produced by hypothalamus. Glucocorticoids have negative feedback control on ACTH and CRF secretion.

Mineralocorticoid release is controlled by the renin-angiotensin system.

Indications for Corticosteroid Therapy

a. Replacement therapy

1. **Acute adrenal insufficiency:** Hydrocortisone or dexamethasone is given IV.
2. **Chronic adrenal insufficiency (Addison's disease):** Hydrocortisone given orally is the most commonly used drug along with adequate salt and water allowance.

3. *Congenital adrenal hyperplasia (adrenogenital syndrome)*: Treatment is to give hydrocortisone 0.6 mg/kg daily in divided doses round the clock to maintain feedback suppression of pituitary.
 - b. Pharmacotherapy**: The following **general principles** must be observed.
 1. A single dose (even excessive) is not harmful.
 2. Short courses (even high dose) are not likely to be harmful in the absence of contraindications; starting doses can be high in severe illness.
 3. *Long-term use is potentially hazardous*: Keep the duration of treatment and dose to minimum.
 4. Initial dose depends on severity of the disease; start with a high dose in severe illness—reduce gradually as symptoms subside, while in mild cases start with the lowest dose and titrate upwards to find the correct dose.
 5. No abrupt withdrawal after a corticoid has been given for > 2 to 3 weeks: May precipitate adrenal insufficiency.
 6. Infection, severe trauma or any stress during corticoid therapy—increase the dose.
 7. Use local therapy (cutaneous, inhaled, intranasal, etc.) wherever possible.
 - 1. Arthritides**
 - i. *Rheumatoid arthritis*: Corticosteroids are indicated only in severe cases as adjuvant to NSAIDs.
 - ii. *Osteoarthritis*: Intra-articular injection of a steroid may be used to control an acute exacerbation.
 - iii. *Rheumatic fever*: Only in severe cases.
 - iv. *Gout*: Intra-articular injection of a soluble glucocorticoid is preferable to systemic therapy.
 - 2. Collagen diseases**: Most cases of systemic lupus erythematosus, polyarteritis nodosa, dermatomyositis, nephrotic syndrome, glomerulonephritis and related diseases need corticoids. Therapy is generally started with high doses which are tapered to maintenance dose when remission occurs.
 - 3. Severe allergic reactions**: Anaphylaxis, angioneurotic edema, urticaria and serum sickness.
 - 4. Autoimmune diseases**: Autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, active chronic hepatitis respond to corticoids.
 - 5. Bronchial asthma**: Inhaled glucocorticoid therapy is now recommended in most cases needing inhaled β_2 agonists.
 - 6. Other lung diseases**: Aspiration pneumonia and pulmonary edema from drowning.
 - 7. Infective diseases**: Corticosteroids are indicated only in serious infective diseases to tide over crisis or to prevent complications.
 - 8. Eye diseases**: Topical instillation as eye drops or ointment is effective in diseases of the anterior chamber—allergic conjunctivitis, iritis, iridocyclitis, keratitis, etc.
 - 9. Skin diseases**: Topical corticosteroids are widely employed and are highly effective in many eczematous skin diseases. Systemic therapy is needed (may be life-saving) in pemphigus vulgaris, exfoliative dermatitis, Stevens-Johnson syndrome and other severe afflictions.
 - 10. Intestinal diseases**: Ulcerative colitis, Crohn's disease, celiac disease.
 - 11. Cerebral edema** due to tumors, tubercular meningitis, etc., responds to corticoids. A short course of 2–4 week oral prednisolone can hasten recovery from Bell's palsy and acute exacerbation of multiple sclerosis. In the latter, methyl prednisolone 1 g IV daily for 2–3 days may be given in the beginning. Neurocysticercosis: Prednisolone 40 mg/day or equivalent is given for 2–4 weeks to suppress the reaction to the dying larvae.
 - 12. Malignancies**: Corticoids are an essential component of combined chemotherapy of acute lymphatic leukemia, Hodgkin's and other lymphomas, because of their marked lympholytic action in these conditions.
 - 13. Organ transplantation and skin allograft**: High dose corticoids are given along with other immunosuppressant to prevent rejection reaction followed by low maintenance dose.
 - 14. Septic shock**: Low-dose (hydrocortisone 100 mg TDS IV infusion for 5–7 days) therapy is needed in patients who are adrenal deficient and require vassopressor drug despite adequate fluid replacement.
 - 15. Thyroid storm**: Corticosteroids reduce peripheral T4 to T3 conversion. Hydrocortisone 100 mg TDS may improve outcome.
 - 16. To test adrenal-pituitary axis function**: Dexamethasone suppresses adrenal-pituitary axis at doses which do not contribute to steroid metabolites in urine—responsiveness of the axis can be tested by measuring daily urinary steroid metabolite excretion.
- Q. 2. Write a short note on adverse effects of corticosteroids.** (TNMGR, Nov. 2001)
- Ans.**
- a. Adverse effects of mineralocorticoids**
 1. Sodium and water retention.
 2. Edema.

3. Hypokalemic alkalosis.
4. Progressive rise in blood pressure.

b. Adverse effects of glucocorticoids

1. *Cushing habitus*: Round face, narrow mouth, supraclavicular hump, truncal obesity, thin limbs.
2. *Skin changes*: Fragile skin, purple striae, easy bruising, telangiectasis, hirsutism, cutaneous atrophy.
3. Hyperglycemia.
4. Muscular weakness.
5. Susceptibility to infections.
6. Delayed healing.
7. Peptic ulceration.
8. Osteoporosis.
9. Posterior subcapsular cataract.
10. Glaucoma.
11. Growth retardation.
12. Fetal abnormalities.
13. Psychiatric disturbances.
14. Suppression of hypothalamo-pituitary-adrenal (HPA) axis.

Q. 3. Write a short note on methylprednisolone.

(TNMGR, April 2012)

Ans. Slightly more potent and more selective than prednisolone: 4–32 mg/day oral. Methylprednisolone acetate has been used as a retention enema in ulcerative colitis. Pulse therapy with high dose methylprednisolone (1 g infused IV every 6–8 weeks) has been tried in nonresponsive active rheumatoid arthritis, renal transplant, pemphigus, etc. with good results and minimal suppression of pituitary-adrenal axis. The initial effect of methylprednisolone pulse therapy (MPPT) is probably due to its anti-inflammatory action, while long-term benefit may be due to temporary switching off of the immune-damaging processes as a consequence of lymphopenia and decreased Ig synthesis.

Q. 4. Classify sympathomimetic drugs based on its therapeutic use.

Ans.

1. **Direct sympathomimetic**: They act directly as agonists on α and/or β adrenoceptors—Adr, NA, and isoprenaline, phenylephrine, methoxamine, xylometazoline, salbutamol and many others.
2. **Indirect sympathomimetic**: They act on adrenergic neuron to release NA, which then acts on the adrenoceptors—tyramine, amphetamine.
3. **Mixed action sympathomimetic**: They act directly as well as indirectly—ephedrine, dopamine, mephentermine.

Q. 5. Describe the pharmacological actions of adrenaline.

(TNMGR, April 2000)

Ans. The overall actions are:

1. **Heart**: Adr increases heart rate.
2. Certain anesthetics (chloroform, halothane) sensitize the heart to arrhythmic action of Adr.
3. **Blood vessels**: Both vasoconstriction (α) and vasodilatation (β_2) can occur depending on the drug, its dose and vascular bed.
4. **BP**: Adr given by slow IV infusion or s.c. injection causes rise in systolic but fall in diastolic BP. Rapid IV injection of Adr (in animals) produces a marked increase in both systolic as well as diastolic BP.
5. **Respiration**: Adr is potent bronchodilators (β_2). Toxic doses of Adr cause pulmonary edema by shifting blood from systemic to pulmonary circuit.
6. **Eye**: Mydriasis occurs due to contraction of radial muscles of iris. The intraocular tension tends to fall, especially in wide angle glaucoma.
7. **GIT**: In isolated preparations of gut; relaxation occurs through activation of both α and β receptors.
8. **Bladder**: Detrusor is relaxed (β) and trigone is constricted (α)—both actions tend to hinder micturition.
9. **Uterus**: Adr can both contract and relax uterine muscle, respectively through α and β receptors.
10. **Splenic capsule**: Contracts (α) and more RBCs are poured in circulation.
11. **Skeletal muscle**: Neuromuscular transmission is facilitated.
12. **CNS**: Adr in clinically used doses, does not produce any marked CNS effects because of poor penetration in brain, but restlessness, apprehension and tremor may occur.
13. **Metabolic**: Adr produces glycogenolysis \rightarrow hyperglycemia, hyperlactacidemia; lipolysis \rightarrow rise in plasma free fatty acid (FFA), calorogenesis and transient hyperkalemia followed by hypokalemia due to direct action on liver, muscle and adipose tissue cells.

Q. 6. Write brief note on glucocorticoids.

(TNMGR, April 2001)

Ans. Actions of glucocorticoids are

1. **Carbohydrate and protein metabolism**: Glucocorticoids promote gluconeogenesis. They also cause protein breakdown—responsible for muscle wasting, lympholysis, loss of osteoid from bone and thinning of skin.
2. **Fat metabolism**: Promote lipolysis due to glucagon, growth hormone, Adr and thyroxine. Redi-

tribution of body fat occurs, which is deposited over face, neck and shoulder—'moon face', 'fish mouth', 'buffalo hump'.

3. **Calcium metabolism:** They inhibit intestinal absorption and enhance renal excretion of Ca^{2+} , also loss of calcium from bone indirectly due to loss of osteoid.
4. **Water excretion:** Effect on water excretion is independent of action on Na^+ transport; hydrocortisone and other glucocorticoids, but not aldosterone, maintain normal GFR
5. **CVS:** Glucocorticoids restrict capillary permeability; maintain tone of arterioles and myocardial contractility.
6. **Skeletal muscles:** Weakness occurs in both hypo- and hypercorticism.
7. **CNS:** Mild euphoria increased motor activity, insomnia, and hypomania or depression.
8. **Stomach:** Aggravate peptic ulcer.
9. **Lymphoid tissue and blood cells:** Glucocorticoids enhance the rate of destruction of lymphoid cells (T cells are more sensitive than B cells).
10. **Inflammatory responses:** Inflammatory response is suppressed by glucocorticoids.
Glucocorticoids interfere at several steps in the inflammatory response; the most important mechanism is limitation of recruitment of inflammatory cells and production of proinflammatory mediators like PGs, LTs, and PAF through inhibition of phospholipase A_2 .
11. **Immunological and allergic responses:** Glucocorticoids impair immunological competence. They suppress all types of hypersensitization and allergic phenomena.

Q. 7. Write a short note on long acting glucocorticoids. (TNMGR, Aug. 2004)

Ans.

1. **Dexamethasone:** Very potent and highly selective glucocorticoid. Long acting, causes marked pituitary-adrenal suppression, but fluid retention and hypertension are not a problem. It is used for inflammatory and allergic conditions 0.5–5 mg/day oral. Shock, cerebral edema, etc. 4–20 mg/day IV infusion or IM injection. Also used topically.
2. **Betamethasone:** Similar to dexamethasone, 0.5–5 mg/day oral, 4–20 mg IM, IV injection or infusion, also topical.

Dexamethasone or betamethasone is preferred in cerebral edema and other states in which fluid retention must be avoided.

Q. 8. Describe the role of corticosteroids in oral medicine/oral lesions.

(RGUHS, April, 2008; TNMGR, March 2009)

Ans.

a. Topical corticosteroids

1. **Agents used:** Beclomethasone (50–100 μg spray). Betamethasone (0.1% cream), clobetasol (0.05% cream), fluocinonide (0.05% cream).
2. **Conditions treated:** Severe recurrent aphthous stomatitis, Behcet's syndrome, pemphigus vulgaris, pemphigoid, oral lichen planus.

b. Injectable corticosteroids

1. **Agents used:** Triamcinolone acetonide (10 mg/ml), dexamethasone (4 mg/ml).
2. **Conditions treated:** Severe recurrent aphthous stomatitis, major aphthous stomatitis, and erosive lichen planus.

c. Systemic corticosteroids

1. **Agents used:** Prednisolone (1 mg/kg body weight)
2. **Conditions treated:** Severe recurrent aphthous stomatitis, Behcet's syndrome, pemphigus vulgaris, pemphigoid, erythema multiforme.

Q. 9. Write a short note on adverse effect of prednisolone. (RGUHS, April, 2007)

Ans.

1. Dyspepsia.
2. Candidiasis.
3. Myopathy.
4. Osteoporosis.
5. Adrenal suppression.
6. Cushing's syndrome.
7. Euphoria.
8. Depression.
9. Peptic ulceration with perforation.

11. EMERGENCY DRUGS IN DENTAL PRACTICE

Q. 1. Discuss in detail emergency drugs used in dental practice.

(TNMGR, March 2010; MUHS, May 2010; UP, April 2014)

Ans. Drugs that should be promptly available to the dentist can be divided into two categories. The first category represents those which may be considered essential. The second category contains drugs which are also very helpful and should be considered as part of the emergency kit.

Essential Emergency Drugs

1. **Oxygen:** Oxygen is indicated for every emergency except hyperventilation. This should be done with a clear full face mask for the spontaneously breathing patient and a bag-valve-mask device for the apneic patient. Oxygen should be available in a portable source, ideally in an "E"-size cylinder which holds over 600 liters. If the patient is conscious, or unconscious yet spontaneously breathing, oxygen should be delivered by a full face mask, where a flow rate of 6 to 10 liters per minute is appropriate for most adults. If the patient is unconscious and apneic, it should be delivered by a bag-valve-mask device where a flow rate of 10 to 15 liters per minute is appropriate. A positive pressure device may be used in adults, provided that the flow rate does not exceed 35 liters per minute.
2. **Epinephrine:** Epinephrine is the drug of choice for the emergency treatment of anaphylaxis and asthma which does not respond to its drug of first choice, albuterol or salbutamol. Epinephrine is also indicated for the management of cardiac arrest. As a drug, epinephrine has a very rapid onset and short duration of action, usually 5 to 10 minutes when given intravenously. For emergency purposes, epinephrine is available in two formulations. It is prepared as 1:1,000, which equals 1 mg per ml, for intramuscular, including intralingual, injections. It is also available as 1: 10,000, which equals 1 mg per 10 ml for intravenous injection. These doses should be repeated as necessary until resolution of the event.
3. **Nitroglycerin:** This drug is indicated for acute angina or myocardial infarction. It is characterized by a rapid onset of action. For emergency purposes it is available as sublingual tablets or a sublingual spray. With signs of angina pectoris, one tablet or spray (0.3 or 0.4 mg) should be administered sublingually. Relief of pain should occur within minutes. If necessary, this dose can be repeated twice more in 5-minute intervals. Systolic blood pressures below 90 mm Hg contraindicate the use of this drug.
4. **Injectable antihistamine:** An antihistamine is indicated for the management of allergic reactions. Whereas mild non-life-threatening allergic reactions may be managed by oral administration, life-threatening reactions necessitate parenteral administration.
5. **Albuterol (salbutamol):** A selective β_2 agonist such as albuterol (salbutamol) is the first choice for management of bronchospasm. When administered by means of an inhaler, it provides selective bronchodilation with minimal systemic cardiovascular

effects. It has a peak effect in 30 to 60 minutes, with duration of effect of 4 to 6 hours. Adult dose is 2 sprays, to be repeated as necessary. Pediatric dose is 1 spray, repeated as necessary.

6. **Aspirin:** Aspirin (acetylsalicylic acid) is one of the more newly recognized life-saving drugs, as it has been shown to reduce overall mortality from acute myocardial infarction. The purpose of its administration during an acute myocardial infarction is to prevent the progression from cardiac ischemia to injury to infarction. The lowest effective dose is not known with certainty, but a minimum of 162 mg should be given immediately to any patient with pain suggestive of acute myocardial infarction.
7. **Oral carbohydrate:** An oral carbohydrate source, such as fruit juice or non-diet soft-drink, should be readily available. Whereas this is not a drug, and perhaps should not be included in this list, it should be considered essential. Its use is indicated in the management of hypoglycemia in conscious patients.

Additional Emergency Drugs

1. **Glucagon:** The ideal management of severe hypoglycemia in a diabetic emergency is the intravenous administration of 50% dextrose. Glucagon is indicated if an intravenous line is not in place and venipuncture is not expected to be accomplished, as may often be the case in a dental office. The dose for an adult is 1 mg. If the patient is less than 20 kg, the recommended dose is 0.5 mg.
2. **Atropine:** This antimuscarinic, anticholinergic drug is indicated for the management of hypotension, which is accompanied by bradycardia. The dose recommended is 0.5 mg initially, followed by increments as necessary until one reaches a maximum of 3 mg.
3. **Ephedrine:** This drug is a vasopressor which may be used to manage significant hypotension. It has similar cardiovascular actions compared with epinephrine, except that ephedrine is less potent and has a prolonged duration of action. For the treatment of severe hypotension, it is ideally administered in 5 mg increments intravenously. Intramuscularly it should be given in a dose of 10 to 25 mg.
4. **Corticosteroid:** Administration of a corticosteroid such as hydrocortisone may be indicated for the prevention of recurrent anaphylaxis. Hydrocortisone may also play a role in the management of an adrenal crisis. The prototype for this group is hydrocortisone, which may be administered in a dose of 100 mg as part of the management of these emergencies.

<i>Emergency condition</i>	<i>Signs and symptoms</i>	<i>Treatment</i>	<i>Drug dosage</i>
Allergic reaction (mild or delayed)	Hives, itching, edema, erythema—skin, mucosa, conjunctiva	<ol style="list-style-type: none"> 1. Discontinue all sources of allergy—causing substances 2. Administer diphenhydramine 	Diphenhydramine 1 mg/kg: Oral Child: 10–25 mg QID Adult: 25–50 mg QID
Allergic reaction (sudden onset): Anaphylaxis	Urticaria—itching, flushing, hives, rhinitis, wheezing/difficulty breathing, bronchospasm, laryngeal edema, weak pulse, marked fall in blood pressure, loss of consciousness	This is a true, life-threatening emergency <ol style="list-style-type: none"> 1. Call for emergency medical services 2. Administer epinephrine 3. Administer oxygen 4. Monitor vital signs 5. Transport to emergency medical facility by advanced medical responders 	Epinephrine 1:1000, 0.01 mg/kg every 5 min until recovery or until help arrives—IM/SC
Acute asthmatic attack	Shortness of breath, wheezing, coughing, tightness in chest, cyanosis, tachycardia	<ol style="list-style-type: none"> 1. Sit patient upright or in a comfortable position 2. Administer oxygen 3. Administer bronchodilator 4. If bronchodilator is ineffective, administer epinephrine 5. Call for emergency medical services with transportation for advanced care if indicated 	<ol style="list-style-type: none"> 1. Albuterol—inhaler 2. Epinephrine 1:1000, 0.01 mg/kg every 15 min as needed—IM/SC
Local anesthetic toxicity	Light-headedness, changes in vision and/or speech, metallic taste, changes in mental status—confusion, agitation, tinnitus, tremor, seizure, tachypnea, bradycardia, unconsciousness, cardiac arrest	<ol style="list-style-type: none"> 1. Assess and support airway, breathing, and circulation (CPR if warranted) 2. Administer oxygen 3. Monitor vital signs 4. Call for emergency medical services with transportation for advanced care if indicated 	Supplemental oxygen—mask
Local anesthetic reaction: Vasoconstrictor	Anxiety, tachycardia/palpitations, restlessness, headache, tachypnea, chest pain, cardiac arrest	<ol style="list-style-type: none"> 1. Reassure patient 2. Assess and support airway, breathing, and circulation (CPR if warranted) 3. Administer oxygen 4. Monitor vital signs 5. Call for emergency medical services with transportation for advanced care if indicated 	Supplemental oxygen—mask
Overdose: Benzodiazepine	Somnolence, confusion, diminished reflexes, respiratory depression, apnea, respiratory arrest, cardiac arrest	<ol style="list-style-type: none"> 1. Assess and support airway, breathing, and circulation (CPR if warranted) 2. Administer oxygen 3. Monitor vital signs 4. If severe respiratory depression, establish IV access and reverse with flumazenil 5. Monitor recovery (for at least 2 hours after the last dose of flumazenil) and call for emergency medical services with transportation for advanced care if indicated 	Flumazenil 0.01–0.02 mg/kg (maximum: 0.2 mg) IV/IM

(Contd.)

(Contd.)

Emergency condition	Signs and symptoms	Treatment	Drug dosage
Overdose: Narcotic	Decreased responsiveness, respiratory depression, respiratory arrest, cardiac arrest	1. Assess and support airway, breathing, and circulation (CPR if warranted) 2. Administer oxygen 3. Monitor vital signs 4. If severe respiratory depression, reverse with naxolone 5. Monitor recovery (for at least 2 hours after the last dose of naxolone) and call for emergency medical services with transportation for advanced care if indicated	Naxolone 0.1mg/kg up to 2 mg: IV, IM/SC
Seizure	Warning aura—disorientation, blinking, or blank stare, uncontrolled muscle movements, muscle rigidity, unconsciousness, postictal phase—sleepiness, confusion, amnesia, slow recovery	1. Recline and position to prevent injury 2. Ensure open airway and adequate ventilation 3. Monitor vital signs 4. If status is epilepticus, give diazepam and call for emergency medical services with transportation for advanced care if indicated	Diazepam—IV Child up to 5 yrs: 0.2–0.5 mg slowly every 2–5 min with maximum = 5 mg Child 5 yrs and up: 1 mg every 2–5 min with maximum = 10 mg
Syncope (fainting)	Feeling of warmth, skin pale and moist, pulse rapid initially then gets slow and weak, dizziness, hypotension, cold extremities, unconsciousness	1. Recline, feet up 2. Loosen clothing that may be binding 3. Ammonia inhales 4. Administer oxygen 5. Cold towel on back of neck 6. Monitor recovery	Ammonia in vials—inhale

5. **Morphine:** Morphine is indicated for the management of severe pain which occurs with a myocardial infarction. Advanced cardiac life support recommendations list morphine as the analgesic of choice for this purpose. If an intravenous is not in place, consideration can be given to administering morphine in a dose of approximately 5 mg intramuscularly.

6. **Naloxone:** If either morphine is included in the emergency kit, or opioids are used as part of a sedation regimen, then naloxene should also be present for the emergency management of inadvertent overdose. Doses should ideally be titrated slowly in 0.1 mg increments to effect.

7. **Nitrous oxide:** Nitrous oxide is a reasonable second choice if morphine is not available to manage pain from a myocardial infarction. For management of pain associated with a myocardial infarction, it

should be administered with oxygen, in a concentration approximating 35%, or titrated to effect.

8. **Injectable benzodiazepine:** The management of seizures which are prolonged or recurrent, also known as status epilepticus, may require administration of a benzodiazepine. Adult doses to consider for lorazepam are 4 mg intramuscularly, or midazolam 5 mg intramuscularly. If an intravenous is in place, these drugs should be slowly titrated to effect.

9. **Flumazenil:** The benzodiazepine antagonist flumazenil should be part of the emergency kit when oral or parenteral sedation is used, as these techniques are usually based on effective use of benzodiazepines. Dosage is 0.1 to 0.2 mg intravenously, incrementally.

In addition to having drugs available, a small amount of basic equipment should be readily available. This

includes a stethoscope, blood pressure cuff, an oxygen delivery system, syringes and needles. Dentists should also consider having an automated external defibrillator (AED), as a means to treat cardiac arrest. Usage of this latter piece of equipment is easily learned and only requires strong knowledge of basic CPR with a small amount of additional training.

Q.2. Write a short note on medical emergencies in dentistry.

(See table given on pages 280-281)

Q. Write a short note on syncope and its management.

(RGUHS, May 2010)

Q. Write a short note on anesthetic emergencies.

(RGUHS, October 2008)

Ans. For all emergencies

1. Discontinue the dental treatment.
2. Call for assistance/someone to bring oxygen and emergency kit.
3. Position patient: Ensure open and unobstructed airway.
4. Monitor vital signs.
5. Be prepared to support respiration, support circulation, provide cardiopulmonary resuscitation, and call for emergency medical services (*see* table on previous page).

Biostatistics, Research Methodology and Ethics

1. BIOSTATISTICS

Q. 1. Discuss role of biostatistics in oral health research. (TNMGR, March 2010; RGUHS, May 2011)

Ans. Statistics is a mathematical science pertaining to the collection, analysis, interpretation or explanation, and presentation of data. It is applicable to a wide variety of academic disciplines, from the natural and social sciences to the humanities. **Biostatistics** is the application of **statistics** in biology.

Role of biostatistics in oral health research includes

1. **Assessment:** Identify problems related to the health of populations and determine their extent.
2. **Policy setting:** Prioritize the identified problems, determine possible interventions and/or preventive measures, set regulations in an effort to achieve change, and predict the effect of those changes on the population.
3. **Assurance:** Make certain that necessary services are provided to reach the desired goals, as determined by policy measures, and monitor how well the regulators and other sectors of the society are complying with policy.

Biostatisticians help in protocol development, data management, study implementation, study monitoring, data analysis, and manuscript writing. The aim of biostatistics is to minimize bias and maximize precision.

Q. 2. Write a short note on measures of variability.

Ans. Variability refers to how “spread out” a group of scores is? The terms variability, spread, and dispersion are synonyms, and refer to how spread out a distribution is. There are four frequently used measures of variability: Range, interquartile range, variance, and standard deviation.

Range: The range is simple to compute and is useful when you wish to evaluate the whole of a dataset. It defines the normal limits of a biological characteristic.

Interquartile range: The interquartile range is a measure that indicates the extent to which the central 50% of values within the dataset are dispersed. It is based upon and related to the median. In the same way that the median divides a dataset into two halves, it can be further divided into quarters by identifying the upper and lower quartiles. The inter-quartile range is found by subtracting the lower quartile from the upper quartile. The inter-quartile range provides a clearer picture of the overall dataset by removing/ignoring the outlying values.

Variance: Variability can also be defined in terms of how close the scores in the distribution are to the middle of the distribution. Using the mean as the measure of the middle of the distribution, the variance is defined as the average squared difference of the scores from the mean.

Standard deviation (SD) (Fig. 8.1): The standard deviation is a measure that summarizes the amount by which every value within a dataset varies from the mean. It is the most robust and widely used measure of dispersion since, unlike the range and inter-quartile range; it takes into account every variable in the dataset. A standard deviation close to 0 indicates that the data points tend to be very close to the mean (also called the expected value) of the set, while a high standard deviation indicates that the data points are spread out over a wider range of values. The standard deviation is usually presented in conjunction with the mean and is measured in the same units. In many datasets the values deviate from the mean value due to chance and such datasets are said to display a normal distribution. In a dataset with a normal distribution most of the values are clustered around the mean while relatively

few values tend to be extremely high or extremely low. For datasets that have a normal distribution the standard deviation can be used to determine the proportion of values that lie within a particular range of the mean value. For such distributions it is always the case that 68% of values are less than one standard deviation (1SD) away from the mean value that 95% of values are less than two standard deviations (2SD) away from the mean and that 99% of values are less than three standard deviations (3SD) away from the mean.

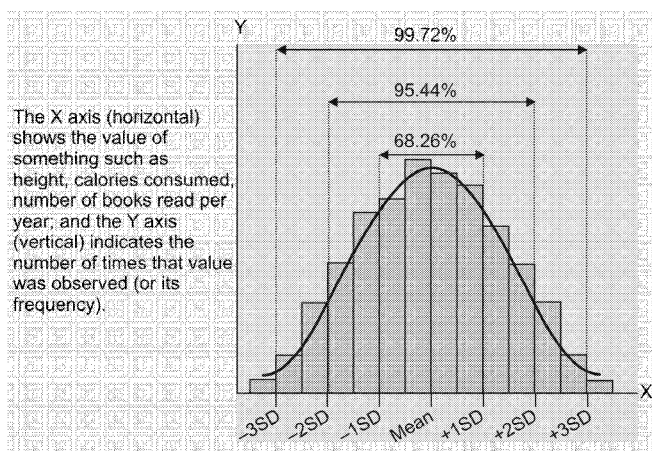


Fig. 8.1: Mean, standard deviation (SD) and degree of freedom (df)

The **sample standard deviation formula** is:

$$S = \sqrt{\frac{\sum(X - \bar{X})^2}{n - 1}}$$

Where,

s = sample standard deviation

Σ = sum of ...

\bar{X} = sample mean

n = number of scores in sample.

Uses of standard deviation

1. It summarises the deviations of a large distribution from mean in one figure used as a unit of variation.
2. Indicates whether the variation of difference of an individual from the mean is by chance.
3. It helps in finding the standard error.
4. It helps in finding the suitable sample size.

Q. 3. Write a short note on student t-test.

(RGUHS, May 2011; HP, May 2013; RUHS, May 2015)

Ans. Student's t-test is a method of testing hypotheses about the mean of a small sample drawn from a normally distributed population when the population standard deviation is unknown. The ratio of observed difference between two means of small samples to the

standard error of difference in the same is denoted by 't'. This ratio follows the 't' distribution. The probability of occurrence of calculated value is determined by reference to 't' table. Probability converted into percentage is stated as level of significance. $P = 0.05$ may be stated as significant at 5% level. If the calculated 't' value exceeds the value given under $P = 0.05$ in the table, it is said to be significant at 5% level and null hypothesis (there is no effective difference between the observed sample mean and the hypothesized or stated population mean, i.e. any measured difference is due only to chance) is rejected and alternate hypothesis is accepted.

Degree of freedom: The quantity in the denominator which is one less than the independent number of observations in a sample is called degrees of freedom (df). It is used in preference of sample size. In unpaired t-test, $df = n_1 + n_2 - 2$; where n_1 and n_2 are the number of observations in each of the two series.

Criteria for applying t-test

1. Random samples.
2. Quantitative data.
3. Variable normally distributed.
4. Sample size less than 30.

Unpaired t-test: This test is applied to unpaired data of independent observations made on individuals of two different or separate group or samples drawn from two populations, to test if the difference between the two means is real or it can be attributed to sampling variability. Following steps are taken to test the significance of difference:

1. Find the observed difference between means of two samples.
2. Calculate the standard error between the two means.
3. Calculate the 't' value.
4. Determine the pooled degrees of freedom.
5. Compare calculated value with the table value at particular degrees of freedom to find the level of significance in two-tailed test. In one-tailed test, compare results with values given under $P = 0.10$ and $P = 0.02$.

Paired t-test: It is applied to paired data of independent observations from one sample only when each individual gives a pair of observations. This test is used:

1. To study the role of a factor or cause when the observations are made before and after its play.
2. To compare the effect of two drugs, given to same individuals in the sample on two different occasions.
3. To study the comparative accuracy of two different instruments.

4. To compare results of two different laboratory techniques.
5. To compare observations made at two different sites in the same body.

Testing by this method eliminates individual sampling variations because the sample is one and the observations on each person in the sample are taken before and after the experiment.

Following steps are taken to test the significance of difference

1. Find the difference in each set of paired observations before and after.
2. Calculate the mean of the difference.
3. Work out the standard deviation (SD) of differences and then the standard error of mean from the same.
4. Determine 't' value.
5. Find the degrees of freedom.
6. Refer 't' table and find the probability of the calculated 't' corresponding to $n-1$ degrees of freedom.
7. If the probability is more than 0.05, the difference observed has no significance. Thus, the factor under study may have no influence on the variable. But if the P is less than 0.05, the difference observed is significant.

Q. 4. Write a short note on chi-square test.

Ans. Chi-square test (χ^2 test), is a non-parametric test, not based on any assumption or distribution of any variable. This test follows chi-square distribution. It is most commonly used when data are in frequencies such as in the number of responses in two or more categories. It has got very important applications as:

1. **Test of proportions:** As an alternate test to find the significance of difference in two or more than two proportions.
 - i. To compare the values of two binomial samples even if they are small, less than 30.
 - ii. To compare the frequencies of two multinomial samples.
2. **Test of association:** It measure the probability of association between two discrete attributes. Two events can often be studied for their association. There are two possibilities, either they influence each other or they do not. In other words, they are either independent of each other or they are dependent on each other. Assumption of independence of each other or no association between events is made, unless proved otherwise by chi-square test. Thus, the test measures the probability or relative frequency of association due to chance and also if the two events are associated or dependent on each other. This test has an advantage that it can be

applied to find association or relationship between two discrete attributes when there are more than two classes or groups.

3. **Test of goodness of fit:** To determine if actual numbers are similar to the expected or theoretical numbers. Whether or not the observed frequencies of a character differ from the hypothetical or expected ones by chance or due to some factor playing part.

Calculation of test: Essential requirement for the calculation are a random sample, qualitative data and lowest expected frequency not less than 5.

1. Make contingency tables. Note the frequencies observed in each class of one event, row-wise and then the numbers in each group of the other event, column wise.
2. Determine the expected number in each group of the sample or the cell of table on the assumption of null hypothesis, i.e. no difference in the proportions of the group from that of the universe.
3. Find the difference between the observed (O) and the expected (E) frequencies in each cell.
4. Calculate values by $= (O-E)^2/E$.
5. Sum up values of all the cells.
6. Calculate the degrees of freedom which are related to the number of categories in both the events. $df = (c-1)(r-1)$; where c is number of vertical columns and r is number of horizontal rows.
7. Refer to Fisher's table. If the calculated value of is higher or lower than the value given in the table, it is significant or insignificant at that particular level of significance to which the reference is made for comparison. Exact level can be determined by comparison with the next higher or lower P value in the table.

Limitations

1. It will not give a reliable result with one degree of freedom if the expected value in any cell is less than 5.
2. Interpret test with caution if sample total or total of values in all the cells is less than 50.
3. This test does not measure the strength of association.
4. The statistical finding of relationship does not indicate the cause and effect.

Q. 5. Discuss tests of significance. (HP, 2013)

Ans. These tests are mathematical methods by which the probability (P) or relative frequency of an observed difference occurring by chance is found. Common tests are Z-test, t-test and χ^2 -test.

Stages in Performing Test of Significance

1. State the null hypothesis of no or chance difference and the alternative.
2. Determine P, i.e. probability of occurrence of estimate by chance, i.e. accept or reject the null hypothesis.
3. Draw conclusion on the basis of P value, i.e. decide whether the difference observed is due to chance or play of some external factors on the sample under study.

Z-test

Application

1. To test the significance of difference between a sample mean and a known value of population.
2. To test the significance of difference between two sample means or between experiment samples mean and control sample mean.

Prerequisite to apply Z-test

1. The samples must be randomly selected.
2. The data must be quantitative.
3. The variable is assumed to follow normal distribution in the population.
4. The sample size must be larger than 30. If SD of population is known, Z-test can still be applied even if the sample is smaller than 30.

When Z-test is applied, the difference observed between a sample estimate and population is expressed in terms of standard error. The score of value of the ratio between the observed difference and standard error (SE) is called 'Z'. If the distance in terms of SE or Z score falls in the zone of acceptance (95% confidence limit), the null hypothesis (H_0) is accepted. The distance from the mean at which is H_0 rejected is called level of significance. Greater the Z value, lesser will be the P. In two-tailed test, the difference is being tested for significance but the direction is not specified. The P value of an experiment group includes both sides of extreme results at both ends of scale. In case of 5% level of significance, probability (P) will be 2.5 % (0.025 at each end). In one-tailed test, one end of the scale is excluded to know specifically whether the results are higher or lower, by specifying the direction on plus or minus side. The significance level or P value will apply to relative end only. The significance level will be half of the P value. In two-tailed test, significance of result is assessed by referring the value given under appropriate P value.

Q. 6. Write about parametric and non-parametric test. (RGUHS, Nov. 2011)

Ans. Parametric tests are also known as normal distribution statistical tests. The statistical methods of inference make certain assumptions about the populations from which the samples are drawn. The statistical techniques which make assumptions about the parameters are called parametric test.

Non-parametric tests are done when

1. The researcher is unaware of the nature of distribution or other required population parameters.
2. When the sample may be too small to test the hypothesis.
3. When scales of measurements are not numerical.

Examples of non-parametric test: Chi-square test, Mann-Whitney U test, Fisher's exact probability test, etc.

Examples of parametric test: t-test, Z-test and ANOVA.

Advantages of non-parametric tests

1. Probability statements obtained from most non-parametric tests are exact probabilities.
2. Can be used for small sample size
3. For treating observations from samples drawn from several different populations.
4. Treat data which are simply classificatory, or the numerical scores having only the strength of ranks.
5. Easier to learn and apply.

Q. 7. Write a short note on ANOVA test.

Ans. Analysis of variance (ANOVA) test or F-test is a collection of statistical models used to analyze the differences among group means and their associated procedures (such as "variation" among and between groups), developed by Ronald Fisher. ANOVAs are useful for comparing (testing) three or more means (groups or variables) for statistical significance. It is used to compare more than two samples drawn from the corresponding normal populations. ANOVA is used in the analysis of comparative experiments, those in which only the difference in outcomes is of interest. The statistical significance of the experiment is determined by a ratio of two variances. This ratio is independent of several possible alterations to the experimental observations.

1. Start with null hypothesis.
2. Calculate the sum of squares.
3. Split this into sum of squares between the classes and sum of squares within the classes.

4. Compare the calculated F-ratio with that given in the F-table at difference between the classes and at difference within the classes at 5% level of significance.
5. If the calculated value is greater than table value, null hypothesis is rejected.

Q. 8. Write about various methods of data collection.

(RGUHS, May 2007; TNMGR, March 2010; BFUHS, May 2011)

Ans. A collective recording of observations either numerical or otherwise is called data. Data is classified into two broad categories:

- a. **Qualitative data:** When the data is collected on the basis of attributes.
- b. **Quantitative data:** When the data is collected through the measurements. It can be discrete or continuous.

The main sources of data are

1. Surveys.
2. Experiments.
3. Records in OPD.

Data can be calculated through

1. **Primary source:** The data is collected by investigator himself.
2. **Secondary source:** The data already recorded is utilized to serve the purpose of the study.

The primary data can be obtained by

1. Direct personal interview.
2. Oral health examination.
3. Questionnaire method.

Q. 9. Write a short note on sampling techniques.

(TNMGR, March 2010; RGUHS, Nov. 2011; MUHS, June 2012)

Ans. Sample means group of individuals who are actually available for the investigations. The objective of sampling are:

1. Estimation of population parameters from the sample statistics.
2. To test the hypothesis about population from which the samples are drawn.

Sampling techniques

1. **Simple random sampling:** In this, every unit in the population has equal chance of being included in the sample.
 - a. Lottery method
 - b. Table of random numbers

This method eliminates personal bias. It necessitates field survey, which enhance the cost and time to collect the data.

2. **Systematic random sampling:** In this systematic sample is formed by selecting one unit at random and then selecting additional units at regular interval. It is simple and convenient to adopt.
3. **Stratified random sampling:** This method is applied when the population is not homogeneous. In this, the population is first divided into homogeneous groups called strata, and the sample is drawn from each stratum at random in proportion to its size. It gives greater accuracy.
4. **Cluster sampling:** This method is used when the population forms natural groups such as villages, wards etc. In this, a sample of clusters is selected, from which entire population is surveyed. It is a simple method, but gives higher standard error.
5. **Multiphase sampling:** In this method, part of the information is collected from the whole sample and part from subsample. This method may be adopted when the interest is in any specific disease.
6. **Pathfinder surveys:** In this sampling of only a specified proportion of the population is done. In this way statistically significant and clinically relevant information is obtained at minimum expense.

Q. 10. Write a short note on estimation of sample size.

(RGUHS, May 2013)

Ans. Sample size should never be small. Bigger the sample size, higher will be the precision of the estimates of samples. Following factors influence the sample size:

1. An approximate idea of the estimate of the characteristics under study and its variability from unit to unit in the population.
2. Knowledge about the precision of the estimate of the characteristic.
3. The probability level within which the desired precision is to be maintained.
4. The availability of experimental material, resources and other practical considerations.

Q. 11. Write a short note on sampling error.

Ans. Sampling error is the deviation of selected sample from the true characteristics, traits, behaviors, qualities or figures of the entire population. They are the errors that creep in due to the sampling process and could arise because of:

1. Faulty sampling design.
2. Small size of the sample.

Non-sampling errors arise due to

1. *Coverage error*: Due to non-response or non-cooperation of the informant.
2. *Observational error*: Due to interviewer's bias or imperfect experimental technique or interaction of both.
3. *Processing errors*: Due to errors in statistical analysis.

Q. 12. Write a short note on sampling bias.

Ans. Sampling is an act of extracting a representative part of population for determining characteristics of whole population. A sample is expected to represent the population.

Sampling bias: Sampling bias is a tendency to favor a selection of sample unit that possess particular characteristics. It may occur in the form of overrepresentation bias.

Types of sampling bias

1. *Self selection bias*: This type of bias happens in a situation when the participants in the study have some control over the study to participate or not.
2. *Exclusion bias*: This type of bias happens when some people of the group are eliminated from the study
3. *Healthy user bias*: This Type of bias occurs when the sample selected has more likelihood to be healthier as compared to general population

Minimizing sampling bias:

1. Large sample size and ensure that the target population is well defined and sample frame should match it as much as possible.
2. Avoid convenient or judgment sampling.
3. When complete population cannot be sampled then care should be taken that the population that is excluded one is not taking away the desired features, which were supposed to be measured from the population.

Q. 13. Write about presentation of statistical data.

(HP, May 2015)

Ans. There are two main methods of presentation of statistical data:

a. Tabulation: The most common way of presenting data in the tables is known as frequency distribution table. The variable has range from lowest to highest. This range is divided into subgroups called classes. The difference between the upper and lower limit of a class is known as class interval.

Rules for making a table

1. Every table should contain a title as to what is depicted in the table.

2. The number of the class intervals should not be too many or too less.
3. The class interval should be at equal width.
4. The class limit should be clearly defined to avoid ambiguity.
5. Each row and column should be clearly defined with the headings.
6. Units of measurements should be specified.
7. If the data is not original, the source of the data should be mentioned at the bottom of the table.

b. Diagram: Diagrams and graphs are extremely useful as they are attractive to eyes, give a bird's eye view, have a lasting impression on mind and facilitate comparison of the data.

Rules for making diagram and graphs

1. Every diagram must be given a title that is self-explanatory.
2. It should be simple and consistent with the data.
3. Values of the variables are presented on horizontal or X-axis and frequency on the vertical line or Y-axis.
4. Diagram should not look clumsy.
5. The scale of the presentation should be mentioned at the right hand top corner of the graph.
6. The scale of division of the two axes should be proportional and the division should be marked along with the details of the variables and frequencies presented on the axes.

Types of diagrams

1. *Bar diagram*: This is used to represent qualitative data. It represents only one variable.
2. *Multiple bar diagram*: This is used to compare qualitative data with respect to a single variable.
3. *Proportional bar diagram*: This is used to represent qualitative data. It is used to compare only proportion of subgroups between different major groups of observations.
4. *Pie diagram*: This shows percentage breakdown of qualitative data.
5. *Component bar diagram*: This is used to represent qualitative data. It is used to represent both, the number of cases in major groups as well as the subgroups simultaneously.
6. *Line diagram*: This is useful to study changes of values in the variable over time.
7. *Histogram*: This is used to depict quantitative data of continuous type. It is a bar diagram without gap between the bars.
8. *Frequency polygon*: This is used to represent frequency distribution of quantitative data and is useful to compare two or more frequency distributions.

9. *Cartograms/spot map*: These maps are used to show geographical distribution of frequencies of a characteristic.

Q. 14. Write a short note on mean, mode, median (measures of central tendency). (RGUHS, May 2011)

Ans. The measures of central position or central tendency are mean, median and mode. They are summary indices describing the central point or the most characteristic value of a set of measurements.

Mean: This implies arithmetic average, which is obtained by summing up all the observations and dividing the total by number of observations.

Median: When all the observations of a variable are arranged in either ascending or descending order, the middle observation is known as median.

Mode: This is the most frequently occurring observation in a series.

Out of these three, mean is better and used more frequently because it uses all the observations in the data and is further used in the tests of significance.

Q. 15. Write a short note on normal curve.

(RGUHS, May 2012)

Ans. If large values are collected for any character, and a frequency table is prepared with small class interval, the frequency curve of this data will give a bell-shaped symmetrical curve, which is known as Gaussian or normal curve. The shape of this curve depends on mean and SD of the data. If the standard deviation (variation) is very high, the width of the curve is also more. Normal curve is used to find confidence limits of the population parameters. Normal distribution also forms the basis for the tests of significance.

Characteristics

1. It is bell-shaped.
2. It is symmetrical.
3. Mean, median and mode coincide.
4. It has two inflections. The central part is convex while at the points of inflection, the curve changes from convexity to concavity. A perpendicular from the point of inflection will cut the base at a distance of one SD from the mean on either side.
5. The shape of the curve tells the probability of occurrence by chance or how often an observation, measured in terms of mean and standard deviation can occur normally in a population.

Q. 16. Write a short note on correlation and regression.

Ans. The relationship between two quantitatively measured variables is called correlation. The extent of

relationship between two sets of figures is called correlation coefficient (r).

Types of correlation

1. *Perfect positive correlation*: In this, the two variables are directly proportional and fully correlated with each other ($r = +1$).
2. *Perfect negative correlation*: The two variables are inversely proportional to each other ($r = -1$).
3. *Moderately positive correlation*: In this, the non-zero values of coefficient lie between 0 and +1 ($0 < r < 1$).
4. *Moderately negative correlation*: In this, the non-zero values of coefficient lie between -1 and 0 ($-1 < r < 0$).
5. *Absolutely no correlation*: In this, the value of correlation coefficient is zero. This indicates that no linear relationship exists between the two variables.

Calculation of correlation coefficient from ungrouped series: When associated variables are normally distributed, the correlation coefficient is called Pearson's correlation coefficient.

Calculation of correlation coefficient from grouped series: When two variables are correlated, but they do not follow the normal distribution, the correlation coefficient used is Spearman's rank order correlation coefficient.

Regression: Regression means change in the measurements of a variable character on the positive or negative side, beyond the mean. Regression coefficient (b) is a measure of the change in one dependent character with one unit change in the independent character. This analysis enables to predict the values of one variable on the basis of the other variable.

Q. 17. Write about hypothesis.

Ans. Hypothesis is a tentative prediction or explanation of the relationship between two or more variables under study. A hypothesis helps to translate the research problem and objectives into clear explanation or prediction of expected results or outcomes of the research study. A clearly stated hypothesis includes the variables to be manipulated or measured, identifies population to be examined and indicates the proposed outcome of the study. Hypothesis also influences the study design, sampling methods, data collection process, and interpretation of the research findings.

Characteristics of a good hypothesis: Conceptual clarity, empirical referents, objectivity, specificity, relevant, testability, consistency, simplicity, availability of techniques, purposiveness, verifiability, profundity of effect, economical.

Sources of hypothesis

1. Theoretical or conceptual frameworks.
2. Previous research.
3. Real life experiences.
4. Academic literature.

Types of hypotheses

1. *Simple hypothesis*: It is the statement that reflects the relationship between two variables.
2. *Complex hypothesis*: It is the statement that reflects the relationship between more than two variables.
3. *Associative hypothesis*: It reflects a relationship between variables that occurs or exists in natural settings without manipulation.
4. *Casual hypothesis*: It predicts the cause and effect relationship between two or more dependent and independent variables in experimental or interventional setting, where independent variable is manipulated by research to examine the effect on dependent variable.
5. *Directional hypothesis*: It specifies not only existence but also the expected direction of the relationship between the variables.
6. *Nondirectional hypothesis*: It reflects the relationship between two or more variables, but it does not specify the anticipated direction.
7. *Null hypothesis*: It is also known as statistical hypothesis and is used for statistical testing and interpretation of statistical outcomes. It states the existence of no relationship between the independent and dependent variables.
8. *Research hypothesis*: It states the existence of relationship between two or more variables.

Q. 18. Write a short note on testing of hypothesis.

Ans. Steps involved in testing of hypothesis

1. State an appropriate null hypothesis for the problem. Calculate the suitable statistics using the standard error—*t*, chi-square, *F*, etc.
2. Determine the degrees of freedom for the statistic.
3. Find the probability level, *P* corresponding to the test statistic using the relevant tables.
4. The null hypothesis is rejected if *P* is less than 0.05; otherwise it is accepted.

In testing of hypothesis, two types of error are possible while accepting or rejecting the null hypothesis

1. *Type I error*: Occurs if the null hypothesis is rejected, when it is actually true.
2. *Type II error*: Occurs if the null hypothesis is accepted, when it is false.

2. RESEARCH METHODOLOGY

Q. 1. Write about principles of research methodology.

(BFUHS, May 2010; RUHS, May 2015)

Ans. All research is different but the following principles are common to all research.

- a. Clear statement of research aims
- b. Information sheet for participants, which sets out clearly, what the research, is about, what it will involve and consent is obtained in writing on a consent form prior to research beginning.
- c. Appropriate methodology
- d. The research should be carried out in an unbiased fashion.
- e. The research should have appropriate and sufficient resources in terms of people, time, transport, money, etc. allocated to it.

The people conducting the research should be trained in research and research methods and this training should provide:

- i. Knowledge around appropriate information gathering techniques.
- ii. An understanding of research issues.
- iii. An understanding of the research area.
- iv. An understanding of the issues around dealing with vulnerable social care clients, especially regarding risk, privacy and sensitivity and the possible need for support.

Those involved in designing, conducting, analyzing and supervising the research should have a full understanding of the subject area. If applicable, the information generated from the research will inform the policy-making process. All research should be ethical and not harmful in any way to the participants.

Q. 2. How to prepare a research protocol?

Ans. A research proposal is a detailed description of a proposed study designed to investigate a given problem. The elements of a research proposal are highlighted below:

1. **Title**: It should be concise and descriptive. It must be informative and catchy.
2. **Abstract**: It is a brief summary of approximately 300 words. It should include the main research question, the rationale for the study, the hypothesis (if any) and the method. Descriptions of the method may include the design, procedures, the sample and any instruments that will be used.
3. **Introduction**: The introduction provides the background information. It should answer the question of why the research needs to be done and what will be its relevance. The introduction typically begins

with a statement of the research problem in precise and clear terms. It allows the investigator to describe the problem systematically, to reflect on its importance, its priority in the country and region and to point out why the proposed research on the problem should be undertaken

4. **Objectives:** Research objectives are the goals to be achieved by conducting the research. They may be stated as 'general' and 'specific'. The general objective of the research is what is to be accomplished by the research project. The specific objectives relate to the specific research questions the investigator wants to answer through the proposed study and may be presented as primary and secondary objectives. It is not desirable to put too many objectives or over-ambitious objectives that cannot be adequately achieved.

5. **Variables:** During the planning stage, it is necessary to identify the key variables of the study and their method of measurement and unit of measurement must be clearly indicated. Four types of variables are important in research:

- a. Independent variables.
- b. Dependent variables
- c. Confounding or intervening variables
- d. Background variables.

The objective of research is usually to determine the effect of changes in one or more independent variables on one or more dependent variables.

6. **Questions and/or hypotheses:** A hypothesis can be defined as a tentative prediction or explanation of the relationship between two or more variables. Hypotheses are not meant to be haphazard guesses, but should reflect the depth of knowledge, imagination and experience of the investigator. In the process of formulating the hypotheses, all variables relevant to the study must be identified.

7. **Methodology:** The method section is very important because it tells how you plan to tackle your research problem. The guiding principle for writing the Methods section is that it should contain sufficient information for the reader to determine whether the methodology is sound.

i. **Research design:** The selection of the research strategy is the core of research design and is probably the singlemost important decision the investigator has to make. The choice of the strategy, whether descriptive, analytical, experimental, operational or a combination of these depend on a number of considerations but this choice must be explained in relation to the study objectives.

ii. **Research subjects or participants:** Depending on the type of study the following:

- a. Inclusion or selection criteria.
- b. Exclusion criteria.
- c. Sampling procedure to ensure representativeness and reliability of the sample and to minimize sampling errors.
- d. Use of controls in your study. Some descriptive studies (studies of existing data, surveys) may not require control groups.
- e. Criteria for discontinuation.

iii. **Sample size:** The proposal should provide information and justification about sample size. A larger sample size than needed to test the research hypothesis increases the cost and duration of the study and will be unethical if it exposes human subjects to any potential unnecessary risk without additional benefit. A smaller sample size than needed can also be unethical as it exposes human subjects to risk with no benefit to scientific knowledge.

iv. **Interventions:** If an intervention is introduced, a description must be given of the drugs or devices (proprietary names, manufacturer, chemical composition, dose, frequency of administration) if they are already commercially available. If they are in phases of experimentation or are already commercially available but used for other indications, information must be provided on available pre-clinical investigations in animals and/or results of studies already conducted in humans (in such cases, approval of the drug regulatory agency in the country is needed before the study).

v. **Ethical issues:** Ethical considerations apply to all types of health research. The proposal must describe the measures that will be undertaken to ensure that the proposed research is carried out in accordance with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical research involving Human Subjects.

vi. **The informed consent form (informed decision-making):** A consent form, where appropriate, must be developed and attached to the proposal. It should be written in the prospective subject's mother tongue and in simple language which can be easily understood by the subject.

vii. **Research setting:** The research setting includes all the pertinent facets of the study, such as the population to be studied (sampling frame), the place and time of study.

viii. **Study instruments:** Instruments are the tools by which the data are collected. Descriptions of other

methods of observations like medical examination, laboratory tests and screening procedures is necessary—for established procedures, reference of published work cited but for new or modified procedure, an adequate description is necessary with justification for the same.

8. **Collection of data and analysis:** A short description of the protocol of data collection minimizes the possibility of confusion, delays and errors. The description should include the design of the analysis form, plans for processing and coding the data and the choice of the statistical method to be applied to each data. What will be the procedures for accounting for missing, unused or spurious data?
9. **Monitoring, supervision and quality control:** Detailed statement about the all logistical issues to satisfy the requirements of good clinical practices, protocol procedures, responsibilities of each member of the research team, training of study investigators, steps taken to assure quality control.
10. **Significance of the study:** Indicate how your research will refine, revise or extend existing knowledge in the area under investigation. How will it benefit the concerned stakeholders? What could be the larger implications of your research study? How do you propose to share the findings of your study with professional peers, practitioners, participants and the funding agency?
11. **References:** The proposal should end with relevant references on the subject.
12. **Appendices** include the appropriate appendices in the proposal. Regarding original scales or questionnaires, if the instrument is copyrighted then permission in writing to reproduce the instrument from the copyright holder or proof of purchase of the instrument must be submitted.

Q. 3. Write a short note on case control study.

Ans. The case control is a type of epidemiological observational study. An observational study is a study in which subjects are not randomized to the exposed or unexposed groups, rather the subjects are *observed* in order to determine both their exposure and their outcome status and the exposure status is thus not determined by the researcher. It is a type of observational study in which two existing groups differing in outcome are identified and compared on the basis of some supposed causal attribute. Case control studies are often used to identify factors that may contribute to a medical condition by comparing subjects who have that condition/disease (the “cases”) with patients who do not have the condition/disease but are otherwise similar (the “controls”).

Biases in case control study

1. Selection bias.
2. Bias in investigating controls.
3. Confounding bias.
4. Problems due to overmatching.
5. Analysis bias.

Advantages

1. Efficient sampling of rare disease.
2. Rapid evaluation of chronic disease.
3. Economical.
4. May serve explanatory purpose.

Limitations

1. Not practical for rare exposures.
2. Sampling is prone to systematic error.
3. Historical information often cannot validate.
4. Relevant cofactors may be difficult to control.

Q. 4. Write a short note on cohort studies.

Ans. A cohort is a group of people who share a common characteristic or experience within a defined period (e.g. are born, are exposed to a drug or vaccine or pollutant, or undergo a certain medical procedure). The comparison group may be the general population from which the cohort is drawn, or it may be another cohort of persons thought to have had a little or no exposure to the substance under investigation, but otherwise similar. A **cohort study** is a form of longitudinal study (a type of observational study), it is an analysis of risk factors and follows a group of people who do not have the disease, and uses correlations to determine the absolute risk of subject contraction. Cohort studies can either be conducted prospectively or retrospectively from archived records. In a cohort study, an outcome or disease-free study population is first identified by the exposure or event of interest and followed in time until the disease or outcome of interest occurs. Because exposure is identified before the outcome, cohort studies have a temporal framework to assess causality and thus have the potential to provide the strongest scientific evidence.

Advantages of the cohort study

1. Gather data regarding sequence of events; can assess causality.
2. Examine multiple outcomes for a given exposure.
3. Can calculate rates of disease in exposed and unexposed individuals over time (e.g. incidence, relative risk).
4. Good for investigating rare exposures.

Disadvantages of the cohort study

1. Large numbers of subjects are required to study rare exposures.
2. Susceptible to selection bias.

Disadvantages of prospective cohort study

1. May be expensive to conduct.
2. May require long durations for follow-up.
3. Maintaining follow-up may be difficult.
4. Susceptible to loss to follow-up or withdrawals.

Disadvantage of retrospective cohort study

1. Susceptible to recall bias or information bias.
2. Less control over variables.

Q. 5. Write a short note on cross-sectional studies.

Ans. Cross-sectional study (non-experimental) is a type of observational study that involves the analysis of data collected from a population, or a representative subset, at one specific point in time. Cross-sectional studies differ from case control studies in that they aim to provide data on the entire population under study. Cross-sectional studies are descriptive studies. They can be used to describe odds ratio, absolute risks and relative risks from prevalence. They may be used to describe some feature of the population, such as prevalence of an illness, or they may support inferences of cause and effect. They are often used to assess the prevalence of acute or chronic conditions, or to answer questions about the causes of disease or the results of intervention. Large cross-sectional studies can be made a little or no expense. This is a major advantage over other forms of epidemiological study. A natural progression has been suggested from cheap cross-sectional studies of routinely collected data which suggest hypotheses, to case control studies testing them more specifically, then to cohort studies and trials which cost much more and take much longer, but may give stronger evidence.

Q. 6. Write a note on experimental studies.

Q. Write a short note on randomized controlled trials.
(RGUHS, May 2013)

Ans. The studies under this category are:

a. Randomized controlled trials: A study design that randomly assigns participants into an experimental group or a control group. As the study is conducted, the only expected difference between the control and experimental groups in a randomized controlled trial (RCT) is the outcome variable being studied. It involves the following steps:

- a. Reference population.
- b. Protocol.

- c. Informed consent.
- d. Randomization.
- e. Concealment of allocation.
- f. Measurement of response variable.
- g. Ascertainment of outcome.

Advantages

1. Good randomization will "wash out" any population bias.
2. Easier to blind/mask than observational studies.
3. Results can be analyzed with well known statistical tools.
4. Population of participating individuals are clearly identified.

Disadvantages

1. Expensive in terms of time and money.
2. Volunteer biases: The population that participates may not be representative of the whole.
3. Does not reveal causation.
4. Loss to follow-up attributed to treatment.

b. Field trials

1. *Preventive trials:* When one has to derive disease-free status in a healthy population using preventive techniques, large scale field trials are required.
2. *Risk factor trials:* In this, specific risk factors are averted in groups of population and the reduction in disease incidence observed.

c. Community trials: The whole community is taken as the study group. Control communities in the neighborhood can be selected for comparison.

d. Natural experiments: When natural events lead on to determinants in health.

e. Before and after studies: When no control is available, the past situation can be compared with situation following intervention.

Q. 7. Write a short note on double blind study.

Ans. A blind or blinded experiment is an experiment in which information about the test is kept from the participant until after the test. Bias may be intentional or unconscious. Blinding is of three types:

- a. *Single blind:* When the patient is blind and the investigator is only aware of the drug given.
- b. *Double blind:* When the patient and the investigator are blind.
- c. *Triple blind:* When the patient, investigator and data clean-up people are blind. If both tester and subject are blinded, the trial is a **double-blind** experiment. Blind testing is used wherever items are to be

compared without influences from tester's preferences or expectations.

The main advantage to a double-blind study is that there is more confidence that any differences between the treatment and the placebo are real, since the perceptions of the doctors, patients and data analysts do not factor into the results. A double-blind study is an unbiased experiment which gives an accurate idea of the benefits of a drug. This is especially important when considering drug treatments that may have side effects or be otherwise detrimental to the patient.

Q. 8. Write a short note on sensitivity and specificity.

Ans. **Sensitivity** is the ability of a test to correctly classify an individual as 'diseased', i.e. probability of being test positive when disease present.

Sensitivity = $a/a + c$; a (true positive), c (false negative).

Specificity is the ability of test to correctly classify an individual as disease-free, i.e. probability of being test negative when disease absent.

Specificity = $d/b + d$; d (true negative), b (false positive).

Positive predictive value: It is the percentage of patients with a positive test who actually have the disease.

$$PPV = a/a + b$$

Negative predictive value: It is the percentage of patients with a negative test who do not have the disease.

$$NPV = d/c + d$$

3. ETHICS

Q. 1. Discuss ethics in dentistry.

Ans. The word 'ethics' is derived from the Greek word 'ethos' meaning custom or character. Ethics in the philosophy of human conduct, a way of stating and evaluating principles by which problems of behavior can be solved. Dental ethics means moral duties and obligations of the dentist towards his patients, professional colleagues and to the society.

History: The "Hippocratic Oath" has been regarded as a summing up of a standard of professional ethics. It is widely believed that the oath was written by Hippocrates, the father of medicine, in the 4th century BC.

In India, the Dentist Act was amended via Section 17A empowering the Dental Council of India to prescribe standards of professional conducts and

etiquette. The code of ethics was framed by the Dental Council in 1975 and later notified by the Government of India as "Dentists (code of ethics) Regulations 1976". It is in force from August 1976.

Ethical Principles

1. To do no harm (non-maleficence).
2. To do good (beneficence).
3. Respect for persons.
4. Justice.
5. Veracity or truthfulness.
6. Confidentiality.

Ethical Rules for Dentists (Prescribed By the DCI)

i. The duties and obligations of dentist towards the patients

1. Every dentist should be courteous, sympathetic, friendly and helpful.
2. He should observe punctuality in fulfilling his appointments.
3. He should establish a well-merited reputation for professional ability and fidelity.
4. The welfare of the patient should be conserved to the utmost of the practitioner's ability.
5. A dentist should not permit considerations of religion, nationality, race, party politics or social standing to intervene between his duties and his patients.
6. Information of a personal nature which may be learned about or directly from a patient in the course of dental practice should be kept in the utmost confidence. It is also the obligation of the dentist to see his auxiliary staff observe this rule.

ii. Duties of dentists towards one another

1. Every dentist should cherish a proper pride in his/her colleagues and should not disparage them either by act or word.
2. When the dentist is interested with the care of the patient of other during sickness or absence, mutual arrangements should be made regarding remuneration.
3. A dentist called upon in any emergency to treat the patient of another dentist, should, when the emergency is provided for retire in favor of the regular dentist but shall be entitled to charge the patient for his services.
4. If a dentist is consulted by the patient of another dentist and the former finds that the patient is suffering from previous faulty treatment, it is his duty to institute correct treatment at once with as

little comments as possible and in such a manner to avoid reflection on his predecessor.

iii. Duties of dentists to the public: Dentist has to assume a leadership role in the community on matters related to dental health.

iv. Some unethical practices

1. Practice by unregistered persons employed by the dentist.
2. Dentist signed under his name and authority issuing any certificate which is untrue, misleading or improper.
3. Dentist advertising whether directly or indirectly, for the purpose of obtaining patients or promoting his own professional advantage.
4. Use of bogus diplomas, etc.
5. Allowing commission.
6. Paying or accepting commissions.
7. Undercutting of charges in order to solicit patients.
8. If the planned treatment is beyond the dentist's skill, the patient is not referred to a consultant.
9. In case of any emergency, consultation during the temporary absence of the patient's dentist, temporary service is provided and the patient is not sent back.
10. If consulted, the dentist accepts charge of the case without request of the referring dentist.

Ethics in Research (UHRS, May 2012): The Nuremberg code is a set of research ethical principles for human experimentation set as a result of the Nuremberg trials at the end of the Second World War. It was the first international instrument on the ethics of medical research, promulgated in 1947. The code, designed to protect the integrity of the research subject, set out conditions for the ethical conduct of research involving human subjects emphasizing their voluntary consent to research.

1. The voluntary informed consent of the human subject is absolutely essential. The duty and responsibility for ascertaining the quality of the consent rest upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.
2. The experiment should be such as to yield fruitful results for the good of the society unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or

other problem under study that the anticipated results justify the performance of the experiment.

4. The experiment should be so conducted to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is a prior reason to believe that death or disabling injury will occur.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability or death.
8. The experiment should be conducted only scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of experiment, the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
10. During the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgement required of him, that a continuation of the experiment is likely to result in injury or disability or death to the experimental subject.

The Hippocratic Oath: The Hippocratic Oath is an oath historically taken by physicians. Hippocrates is often called the father of medicine in Western culture.

Modern version: I swear to fulfil, to the best of my ability and judgment, this covenant:

I will respect the hard-won scientific gains of those physicians in whose steps I walk, and gladly share such knowledge as is mine with those who are to follow.

I will apply, for the benefit of the sick, all measures which are required, avoiding those twin traps of overtreatment and therapeutic nihilism.

I will remember that there is art to medicine as well as science, and that warmth, sympathy, and understanding may outweigh the surgeon's knife or the chemist's drug.

I will not be ashamed to say "I know not," nor will I fail to call in my colleagues when the skills of another are needed for a patient's recovery.

I will respect the privacy of my patients, for their problems are not disclosed to me that the world may know. Most especially must I tread with care in matters of life and death. If it is given me to save a life, all thanks. But it may also be within my power to take a life; this awesome responsibility must be faced with great humility and awareness of my own frailty. Above all, I must not play at God.

I will remember that I do not treat a fever chart, a cancerous growth, but a sick human being, whose illness may affect the person's family and economic stability. My responsibility includes these related problems, if I am to care adequately for the sick.

I will prevent disease whenever I can, for prevention is preferable to cure.

I will remember that I remain a member of society, with special obligations to all my fellow human beings, those sounds of mind and body as well as the infirm.

If I do not violate this oath, may I enjoy life and art, respected while I live and remembered with affection thereafter. May I always act so as to preserve the finest traditions of my calling and may I long experience the joy of healing those who seek my help.

4. COMPUTERS AND LASERS

Q. 1. Write about applications of computers in dentistry.

Ans. Everything done in dentistry, that involves research, teaching, administration or patient care is based on generation, storage and manipulation of the information. Computers are capable of handling large amount of such data. In practice management, besides the usual collecting, sorting and searching of data, productivity and efficiency are greatly increased through computer appointments, recall and practice analysis programmes. In patient education, the use of computer graphics has enabled simulation of cosmetic changes to be presented to the patient with before and after possibilities. Dental education and communications have moved forward with the introduction of Computer Assisted Instruction Programmes, and bibliographic databases including electronic transmission of Continuing Dental Education which are now easily available. In the field of Diagnostics and Treatment planning, the advent of CAD-CAM has made possible the use of cutting devices which mills a 3-dimensional model of the designed restoration from solid blocks of gold. Computer applications have also been used in forensic dentistry where identification systems describe tooth conditions and other oral characteristics besides automated screening and

matching of antemortem databases. In the field of dentistry, computers are used for a large number of purposes. They can be broadly classified as:

1. Administrative applications
2. Clinical applications
3. Other applications

1. Administrative applications: Computers are used in the administration field. They are aimed for a smooth running of dental clinics, hospitals and dental institutions. The various activities which are part of administrative applications are mentioned below.

- Patient appointments and recalls.
- Correspondence.
- Billing and accounting.

Inventory controls and supply orders.

- Dental insurance claims.
- Document preparation and word processing.
- Referral information.
- Missed appointments and follow ups.

Clinical applications: Computers are also very much useful for the dentist in their professional practice.

- Patient records storage and retrieval.
- Patient evaluation, examination and treatment planning.
- Patient motivation and awareness.
- Appliance designing using **CAD, CAM techniques**.
- Storage of patient photographs, radiographs and study models.
- Computerized imaging techniques.
- Computerized cephalometrics.
- Growth prediction.
- Radiovisiography (RVG) technique.
- Clinical diagnosis and treatment planning.

Other applications: Besides administrative purposes and clinical uses, the other applications include:

- Creating a database of **survey** information.
- Case presentations.
- Conference presentations.
- Reviewing of literature.
- Continuing medical education.

Q. 2. Write about LASERS in dentistry.

Ans. LASER is an acronym for light amplification by stimulated emission of radiation. Lasers are heat producing devices converting electromagnetic energy into thermal energy. The characteristic of a laser depends on its wavelength (WL), and wavelength affects both the clinical applications and design of laser.

The WL used in medicine and dentistry generally range from 193 to 10600 nm, representing a broad-spectrum from ultraviolet to the far infra-red range.

Mechanism of action: If radiation energy is absorbed by the tissue, following reactions occur.

1. **Photochemical interaction:** This type of interaction includes the interaction of the beam with the chemical process of the tissue and includes:
 - a. *Biostimulation:* It describes the stimulatory effect of laser light on biochemical and molecular processes that normally occur in tissue like healing and repair.
 - b. *Photodynamic therapy:* It is the therapeutic use of lasers for the treatment of pathological conditions. This could be beneficial in treating potentially premalignant lesions.
 - c. *Fluorescence:* This can be used to detect light reactive substances in the tissues.
2. **Photothermal interaction:** It includes the following:
 - a. *Photoablation:* This is removal of the tissue by vaporization and superheating of the tissue fluids, coagulation or hemostasis.
 - b. *Photopyrolysis:* It is burning away of the tissues.
3. **Photomechanical interaction:** It includes the following:
 - a. *Photodisruption or photodissociation:* It is breaking apart of the structure by laser light.
 - b. *Photoacoustic:* This involves removal of the tissues with shockwave therapy.
4. **Photoelectrical interaction:** It includes the following:
 - a. *Photoplasmolysis:* In this the tissue is removed through the formation of electrically charged ions.

Types of laser: Based on power, lasers can be classified into the following three categories:

1. **High-power lasers (hard, hot):** These lasers increase tissue kinetic energy and produce heat. As a result, they leave their therapeutic effects through thermal interactions. These effects include necrosis, carbonization, vaporization, coagulation and denaturation. These lasers usually have an output power of more than 500 mW.
2. **Intermediate-power lasers:** These lasers leave their therapeutic effects without producing significant heat. To shorten treatment period length and to accelerate the therapeutic effect in some cases, low-power lasers are replaced by intermediate lasers with output powers ranging from 250 to 500 mW.
3. **Low-power lasers (soft, cold):** These are also known as **low level lasers**. These lasers have no thermal

effect on tissues and produce a reaction in cells through light, called photobiostimulation or photobiochemical reaction. Output power of these lasers is less than 250 mW.

Lasers Used

1. **Carbon dioxide laser:** This is most commonly used in soft tissue surgeries. It has a wavelength of 10,600 nm and is readily absorbed by water. Therefore, it does not penetrate too deep into the tissues (0.1–0.23 mm) without repeated or prolonged use. This is used ideally for superficial lesions, resurfacing of the skin and removal of sialoliths.
2. **Nd:YAG laser:** It has a wavelength of 1,064 nm. This is mostly used in soft tissue procedures. It is also used in removing tattoos and certain pigmented lesions.
3. **Ho:YAG laser:** This is used for arthroscopic surgery, soft tissue surgery. It has a wavelength of 2,100 nm.
4. **Er:YAG lasers:** These lasers are most commonly used for the treatment of hard tissues and skin resurfacing. They have a wavelength of 2944 nm.
5. **Argon lasers:** They have a wavelength of 488,514 nm are readily absorbed by hemoglobin and melanin and are useful in the treatment of pigmented lesions and vascular anomalies.
6. **Diode lasers:** They have a wavelength of 620 to 900 nm and are used to treat oral soft tissue lesions.

Applications of Laser in Oral Medicine

a. Oromucosal pathologies

1. **Leukoplakia:** The lesions can be removed with laser and encourages regeneration of new, healthy epithelium. Small lesions can be removed with a carbon dioxide laser with a margin of 3 to 4 mm. The decision of whether excision or vaporization should be done is based on the texture and thickness of the lesion. Thickened hyperkeratotic lesions have less water content; therefore, vaporization cannot be done. Diffuse lesions cannot be managed by excision. The disadvantage of vaporization is that, a specimen cannot be taken and sent for pathological examination.
2. **Oral lichen planus:** Erosive lichen planus can be controlled by laser treatment. Carbon dioxide laser should be used along with selected local and systemic medications. The contact Nd:YAG laser with round probe can also be used.
3. **Oral submucous fibrosis:** The use of laser to release fibrotic bands leads to healing with minimal scarring, thereby decreasing the probability of procedure induced trismus. Diode laser is a portable device

which delivers rays through a fiberoptic cable, and hence, can be delivered to relatively 'difficult to access' areas. Its cutting depth is less than 0.01 mm, and thus preserves tissues beyond this depth. It gives a precise line of controlled cutting without damaging the muscles and deeper structures.

4. *Herpes simplex virus infections*: Low level laser therapy (LLLT) can be used in association with conventional therapy. The choice of treatment method will depend on the number, location and size of the lesions. LLLT presents both anti-inflammatory and analgesic effects, contributing to tissue repair and fibroblast proliferation and an increase in the interval between infections.
5. *Recurrent aphthous ulcers*: Recently, LLLT has been used as the treatment modality. It helps in immediate pain relief and accelerates wound healing. Cold lasers (LLLT lasers) accelerate wound healing and reduce pain by perhaps stimulating oxidative phosphorylation in mitochondria and modulating inflammatory responses.

b. Orofacial pain

1. *Trigeminal neuralgic pain*: Low-level laser of 830 nm wavelength is efficient in the treatment of neuralgic pain.
2. *Myofacial pain*: Use of 830 nm wavelength laser in several appointments can reduce or eliminate myofacial pain.
3. *Temporomandibular joint disorder pain*: A potential noninvasive treatment for TMJ pain is LLLT. The efficacy of LLLT to be superior to placebo therapy.
4. *Mucositis pain*: 'Low' or 'low and middle' energy (output power ranged from 5 to 200 mW) irradiation with helium/neon laser (wavelength 632.8 nm) has been reported to be a simple atraumatic technique (with no known toxicity in clinical setting), useful in the treatment of mucositis of various origins.

c. Salivary gland pathologies

1. *Sialolithiasis*: Various types of lasers have been employed to treat sialolithiasis, including carbon dioxide, diode, Ho:YAG and Nd:YAG lasers. Among these diode lasers have been reported to have more advantages. It has a greater absorption by hemoglobin, oxyhemoglobin and melanin, thereby making its penetration depth smaller than Nd:YAG laser.
2. *Mucocele*: CO₂ laser has a high water absorption rate and is well absorbed by all soft tissues with high water content. In addition, its effects on adjacent tissues are minimal. These properties make CO₂ laser the perfect surgical treatment for oral soft tissues. The cut is precise and does not affect the muscle

layer, causes minimal hemorrhage and almost no acute inflammatory reaction. The operation time is short (3 to 5 minutes) making it a convenient treatment for children and patients who cannot withstand long treatment.

d. Biopsy: The laser biopsies present some advantages compared those made with the scalpel: Generally these interventions do not require anesthesia or sutures and the healing of the donor site, at least in the initial stages, it is more rapid. The laser most commonly used for this purposes are the diode laser, KTP laser, CO₂ laser, Nd:YAG laser, Er:YAG laser.

Application of Lasers in Conservative and Endodontics

1. **Caries detection**: The DIAGNOdent is used for caries and calculus detection by emitting a non-ionizing laser beam at a wavelength of 655 nm (at a 90 degree angle) toward a specific darkened groove on the occlusal surface of a patient's tooth where bacterial decay is suspected, or along the long axis of a root surface to detect the presence of bacteria-laden calculus. This diagnostic technology, in which the photons of this laser wavelength are absorbed into any existing bacteria in these areas of the patient's tooth, is called laser-induced fluorescence. The instrument's digital display indicates the number of bacteria in this area of the tooth and may correspond to the extent of decay or existence of calculus.
2. **Cavity preparation**: The Er:YAG laser has been successfully used to prepare holes in enamel and dentine with no cracks and low or no charring.
3. **Caries removal**: Carious material contains a higher water content compared with surrounding healthy dental hard tissues. Consequently, the ablation efficiency of caries is greater than for healthy tissues. There is a possible selectivity in the removal of carious material using the Er:YAG laser because the ablation threshold of healthy dentine is two times higher than the corresponding threshold of carious dentine. The laser removed infected and softened carious dentine to the same degree as the bur treatment. In addition, a lower degree of vibration is noted with the Er:YAG laser treatment.
4. **Restoration removal**: The Er:YAG laser is capable of removing cement, composite resin and glass ionomer. The efficiency of ablation is comparable to that of enamel and dentine. Lasers should not be used to ablate amalgam restorations however, because of potential release of mercury vapor. The Er:YAG laser is incapable of removing gold crowns, cast restorations and ceramic materials because of

the low absorption of these materials and reflection of the laser light.

5. **Etching:** Laser etching has been evaluated as an alternative to acid etching of enamel and dentine. The Er:YAG laser produces micro-explosions during hard tissue ablation that result in microscopic and macroscopic irregularities. These micro-irregularities make the enamel surface micro-retentive and may offer a mechanism of adhesion without acid-etching.
6. **Treatment of dentinal hypersensitivity:** Desensitising of hypersensitive dentine with an Er:YAG laser is effective, and the maintenance of a positive result is more prolonged than with other agents.
7. **Caries prevention:** Laser irradiation of dental hard tissues modifies the calcium to phosphate ratio, reduces the carbonate to phosphorous ratio, and leads to the formation of more stable and less acid soluble compounds, reducing susceptibility to acid attack and caries.
8. **Bleaching:** The objective of laser bleaching is to achieve an effective power bleaching process using the most efficient energy source. Power bleaching has its origin in the use of high-intensity light to raise the temperature of hydrogen peroxide, accelerating the chemical process of bleaching. The FDA approved standards for tooth whitening has cleared three dental laser wavelengths: Argon, CO₂ and the most recent 980 nm GaAlAs diode.
9. **In endodontics:** Lasers are being considered to disinfect root canals photothermally. Lasers may be more effective than medications to break up biofilms by denaturing proteins and volatising the aqueous component. A technique known as photoactivated disinfection (PAD) uses tolonium chloride solution to photosensitise bacterial cells such as *E. faecalis*. These cells then selectively absorb laser light at 635 nm and are ablated. Such a technique has the potential to resolve persistent infections where conventional approaches have failed. Er:YAG laser technology has been used to carry out endodontic therapy from access, to disinfection to root canal preparation without supplemental anesthesia. A further benefit to these lasers when they are preparing the root canal space is that they remove the smear layer.

Applications of Lasers in Periodontology

1. **Periodontal pocket therapy:** Diodes, Er:YAG, Nd:YAG, and CO₂ devices from various manufacturers have received FDA clearance for sulcular debridement, defined as removal of diseased or inflamed soft tissue in the periodontal pocket to improve clinical indices including gingival index, gingival bleeding index, probe depth, attachment level and tooth mobility. Nd:YAG lasers are useful in periodontal care because of their affinity for pigment allows for selective debridement of diseased sulcular epithelium. The Nd:YAG wavelength is also bactericidal, biostimulative, and has the ability to stimulate fibrin formation with the proper parameters. Erbium lasers have been shown to be effective at scaling and root planning, effective pocket decontamination, and can replace scalpels when incisions are needed.
2. **Laser biopsy:** All dental laser wavelengths are capable of performing precise biopsies. Smaller lesions can often be removed with a compounded topical anesthetic only. Sutures are rarely needed due to the excellent hemostasis and minimal trauma observed when lasers are used properly.
3. **Gingivectomy:** Gingivectomy is the most common procedure performed with dental lasers. All laser wavelengths can be used to precisely incise gingiva for restorative, cosmetic, and periodontal indications. Rapid healing and reduced pain are commonly seen postoperatively and patients rarely need periodontal packing or sutures.
4. **Frenectomy:** Frenectomies are a very common laser procedure that can be accomplished effectively with any wavelength. Simple ones can often be achieved with topical anesthesia only. Hemostasis is usually excellent, particularly with the more thermal CO₂, Nd:YAG, and diodes.
5. **Crown-lengthening with minimum trauma.**
6. **Implantology:** A diode laser can be used at second stage surgery instead of a scalpel. The laser cuts precisely and effects hemostasis and seems to minimise pain and swelling. Many laser dentists report that gingival contours seem to be stable after implant recovery procedures, as long as gentle parameters were used to the extent that impression procedures can be carried out immediately.

Applications in Oral Surgery

CO₂ lasers have been popular in oral surgery due to their precise incisions and excellent hemostasis. Erbium lasers are capable of cutting bone in a less traumatic fashion and can be quite useful for the following procedures:

- Surgical extractions with less traumatic flaps and bone removal
- Alveoplasty
- Incision and drainage
- Operculectomies

- Treatment of peri-implantitis
- Pre-prosthetic
 - Ridge preparation/hyperplastic tissue reduction
 - Frenectomies
 - Tuberosity reductions
 - Vestibuloplasty
 - Tori Removal

Nd:YAG and diodes have biostimulative properties that can be used to promote healing, osteogenesis, and postoperative comfort. Nd:YAG lasers can also form fibrin rapidly in an extraction site creating a quick and more durable clot. An interesting application of dental lasers is in the treatment of bisphosphonate induce osteonecrosis of the jaw (BONJ). BONJ occurs because the drugs inhibit osteoclastic activity which is needed whenever bone is surgically manipulated. When the necrotic bone is removed with an Er:YAG laser the remaining bone is so minimally traumatized that osteoclastic needs are minimized. Nd:YAG biostimulation can be used concurrently or separately to promote bone healing as well.

Applications in Pediatric Dentistry

Dental lasers offer many advantages when treating children. All procedures previously discussed apply to pediatric treatments as well. The ability to provide care with less use of needles and high-speed handpieces makes for a less traumatic experience. Behavioral management improves when these frightening devices are not used. Subsequent treatment appointments are

often easier to manage as well when the child has a more positive experience. All previously discussed restorative and surgical procedures can be performed safely on children. Dental lasers can also aid in procedures such as pulpotomies and orthodontic surgical needs.

Advantages

1. Dry surgical field.
2. Better visualization.
3. Tissue surface sterilization.
4. Reduction in bacteremia.
5. Decreased pain.
6. Decreased swelling.
7. Decreased edema.
8. Decreased scarring.
9. Tissues show minimal mechanical trauma.
10. Faster healing response.
11. Widely accepted by patients.
12. The operating time is reduced.
13. Patients require a shorter hospital stay, thus is cost-effective.

Disadvantages

1. Relatively high in cost.
2. Lasers require specialized training.
3. No single wavelength will optimally treat all dental diseases.
4. They are harmful to eyes and skin.

Dental Material

Q. 1. Write a short note on rheological properties of dental materials. (RGUHS, Oct. 2010)

Ans. Rheology is the study of flow of matter.

Properties

1. **Viscosity:** It is the resistance offered by a liquid when placed in motion. It is measured in poise or centipoise.
2. **Creep:** It is defined as time dependent plastic deformation or change of shape that occurs when a metal is subjected to a constant load near its melting point.
 - a. **Static creep:** It is a time dependant deformation produced in a completely set solid subjected to a constant stress.
 - b. **Dynamic creep:** It is produced when the applied stress is fluctuating, such as in fatigue type test.
3. **Flow:** In dentistry, the term flow is used instead of creep to describe the rheology of amorphous substances. For example, waxes.
4. **Behavior of liquids**
 - a. **Newtonian (ideal):** Liquids that exhibit a constant viscosity under all the stress conditions.
 - b. **Pseudoplastic:** Exhibit decrease in viscosity, when there is increase in shear rate.
 - c. **Dilatants.**
5. **Thixotropic:** These materials exhibit different viscosity, after it is deformed.

Q. 2. Write a short note on color and its significance. (TNMGR, Sept. 2010)

Ans. Color is formed by the combined intensities of wavelengths present in a beam of light.

Dimensions of color

1. **Hue:** It refers to basic color of an object. For example, red, green or blue.

2. **Value:** Color can be separated into light and a dark shade, this lightness, which is measured independently of the color hue is called value.
3. **Chroma:** It represents the degree of saturation of a particular hue.

Measurement of color: By Munsell system.

Clinical consideration: Esthetics plays a very important role in modern dental treatment. The ideal restorative material should match the color of the tooth it restores. In maxillofacial prosthetics, the color of the gums, external skin and the eyes have to be duplicated. Clinically in the operatory or dental lab, color selection is usually done by the use of shade guides.

Q. 3. Write a short note on tarnish and corrosion.

(TNMGR, March 2008; BFUHS, May 2011)

Q. Write a short note on heterogeneous corrosion.

(RGUHS, Oct. 2010)

Ans. Tarnish is a surface discoloration on a metal or even a slight loss or alteration of the surface finish or lustre.

Causes

- a. Formation of hard and soft deposits on the surface of the restorations.
- b. Pigment producing bacteria, produce strain.
- c. Formation of thin films of oxides, sulfides and chlorides.

Corrosion is actual deterioration of a metal by reaction with the environment.

Causes: Water[, oxygen, chloride ions, sulfides like hydrogen sulfide or ammonium sulfide in the oral cavity.

Classification

1. **Chemical or dry corrosion:** In this the metal reacts to form oxides, sulfides in the absence of electrolytes.

For example, formation of Ag_2S in dental alloys containing silver.

2. *Electrolytic or electrochemical or wet corrosion*: This requires the presence of water or other fluid electrolytes. There is formation of free electrons and the electrolyte provides the pathway for the transport of electrons. The surface of anode corrodes due to loss of electrons.
 - a. *Galvanic corrosion*: It occurs when dissimilar metals lie in direct physical contact with each other.
 - b. *Heterogeneous corrosion*: It occurs within the structure of the restoration itself. Heterogeneous/mixed compositions can cause the galvanic corrosion. When an alloy containing eutectic is immersed in an electrolyte the metallic grains with the lower electrode potential are attacked and corrosion results. In metals or alloy, the grain boundaries may act as anodes and the interior of grain as the cathode. Solder joints may also corrode due to the inhomogeneous composition. Impurities in any alloy enhance corrosion.
 - c. *Stress corrosion*: A metal which has been stressed by cold working becomes more reactive at the site of maximum stress. If stressed and unstressed metals are in contact in an electrolyte, the stressed metal will become the anode of a galvanic cell and will corrode.
 - d. *Concentration cell or crevice corrosion*
 - i. *Electrolyte concentration cell*: In a metallic restoration which is partly covered by food debris, the composition of electrolyte under the debris will differ from that of saliva and this can contribute to the corrosion of the restoration.
 - ii. *Oxygen concentration cell*: Differences in oxygen tension in between parts of the same restoration causes corrosion of the restoration. Greater corrosion occurs in the part of the restoration having lower concentration of oxygen.

Q. 4. Write a note on tissue conditioners.

(TNMGR, March 2008; April 2013)

Ans. Tissue conditioners are temporary soft liners, used only for a few days.

Uses

1. Poor health conditions, ill fitting dentures.
2. As functional impression material.
3. As reline materials in surgical obturators.
4. Used to stabilize and enhance retention and comfort of denture base during maxillomandibular relation.

Composition

Powder: Polyethylmethacrylate.

Liquid: Aromatic ester in ethanol.

Q. 5. Critically evaluates various types of resins used for provisional restorations. (BFUHS, Nov. 2009)

Ans. These materials have more cross-linking agent as compared to denture base resins.

Composition: Polymethylmethacrylate (PMMA), peroxide, oxide particles, methymethacrylate (MMA) liquid, tertiary amines, hydroquinone.

Uses

1. Used as resin facings or veneer on indirect cast restorations.
2. Used in fabrication of provisional crowns and bridges.
3. Acrylic facings of cast partial denture.
4. Immediate acrylic denture.

Types

1. PMMA resins.
2. Polymethyl (isobutyl) methacrylate resins.
3. Epimines.

Q. 6. Write a short note on elastomers.

(TNMGR, Aug. 2008)

Ans. Types

- a. *According to chemistry*
 1. Polysulfide.
 2. Condensation polymerizing silicones.
 3. Addition polymerizing silicones.
 4. Polyether.
- b. *According to viscosity*
 1. Light body/syringe consistency.
 2. Medium/regular body.
 3. Heavy body/tray consistency.
 4. Very heavy body/putty consistency.

Uses

1. In fixed partial dentures for impressions of prepared teeth.
2. Impressions of dentulous/edentulous mouth.
3. Polyether is used for border moulding.
4. For bite registration.

Properties

1. Excellent reproduction of surface details.
2. They are generally hydrophobic.
3. Good elastic properties.
4. Coefficient of thermal expansion is high.
5. Dimensional changes and inaccuracies may occur.
6. Tear strength is excellent.
7. These can be electroplated.
8. They have poor adherence to impression tray.
9. The shelf-life is of two years.

Q. 7. Write a short note on denture base resins.

(TNMGR, March 2009)

Ans. ISO classification of denture base materials

Type 1: Heat cure polymers: Polymerization at temperature $>65^{\circ}\text{C}$.

Type 2: Self cure polymers: Polymerization at temperature $<65^{\circ}\text{C}$.

Type 3: Thermoplastic materials: Moldable polymers.

Type 4: Light cure materials: Polymerization by visible or UV radiation.

Type 5: Microwave materials: Microwave heat polymerization.

Composition of heat activated acrylic resin

Powder: Polymethylmethacrylate (PMMA), benzoyl peroxide (initiator), mercuric sulfide, cadmium sulfide (color pigment), dibutyl phthalate (plasticizer), zinc oxide, titanium oxide (opacifiers).

Liquid/monomer: Methylmethacrylate (MMA), dibutyl phthalate (plasticizer), hydroquinone (inhibitor), glycol dimethacrylate (cross-linking agent).

Composition of self cure acrylic resin

Powder: Polymethylmethacrylate (PMMA), benzoyl peroxide (initiator), mercuric sulfide, cadmium sulfide (color pigment).

Liquid/monomer: Methylmethacrylate (MMA), tertiary amines (activator), hydroquinone (inhibitor).

Composition of light activated acrylic resin

Polyether urethane dimethacrylate (major component), camphoroquinone (photoinitiator), amine (photo-activator), silicone dioxide (inorganic filler), acrylic resin beads (organic fillers), high molecular weight acrylic resin (monomer).

Q. 8. Write a short note on use and abuse of denture adhesives.

(BFUHS, Nov. 2006; TNMGR, Sept. 2010, Oct. 2011)

Ans. These are highly viscous aqueous solutions which are often used to improve the retention of complete dentures.

Composition: Keraya gum, tragacanth, sodium carboxy methyl cellulose, polyethylene oxide, flavoring agent. They are applied to denture base and inserted. When wet, the polymer portion absorbs water and swells. They improve the retention of the denture base through adhesion. It fills up the spaces between the denture and the tissue. The high viscosity also prevents displacement. They usually have pleasant smell. Most of the components are permitted food additives and generally safe.

Disadvantages

1. Unpleasant feel.
2. Difficult to clean.
3. Diluted easily by saliva.
4. In excess may cause gastric irritation.
5. May be allergic to some patient.
6. May cause caries because of acidic in nature.

Indications:

1. Temporary retention of poorly fitting dentures.
2. Patient with poor neuromuscular control.

Q. 9. Write a short note on bonding primers.

(RGUHS, May 2011)

Ans. Primers contain bifunctional hydrophilic monomers dissolved in solvents such as acetone, ethanol or water. These solvents displace water from the moist collagen network to allow infiltration of monomers through the nanospaces of collagen network. This renders the hydrophilic dentin hydrophobic and spongy for the penetration of the resin into the dentin. For example, HEMA (hydroxyethyl methacrylate), NMSA (N-methacryloyl-5-aminosalicylic acid), NPG (N-phenylglycine), PMDM (pyromellitic-diethyl methacrylate) and 4-META (methacryloxyethyl trimellitic anhydride).

Application of primer: Primers should be applied for at least 15 seconds to allow the monomer to diffuse to the complete depth of demineralized dentin. The primer should be air dried with a blow of oil free compressed air to volatilize any remaining excess solvent before the application of adhesive.

Q. 10. Write a note on biocompatibility of materials.

(TNMGR, March 2009; RGUHS, Nov. 2011)

Q. Write a short note on toxicity evaluation of dental materials.

(TNMGR, March 2008)

Ans. Biocompatibility is defined as the ability of a restorative material to induce an appropriate and advantageous host response during its intended clinical use.

Biocompatibility tests**a. In vitro tests**

1. Direct cell culture.
2. Agar diffusion testing.
3. Filter diffusion testing.
4. Dentin barrier testing.
5. Ames test.
6. Micronucleus test.

b. *Animal tests:*

1. LD₅₀ median lethal dose.
2. Limit test.
3. Implantation test.
4. Maximization test.
5. Buehler test.
6. Micronucleus test.

c. *Usage tests*

1. Pulp/dentin test.
2. Endodontic usage test.
3. Intraosseous implant test.
4. *Clinical trials*
 - a. *Phase I:* Involves few healthy individuals after obtaining consent.
 - b. *Phase II:* Involves a small group of patients.
 - c. *Phase III:* Large scale study.
 - d. *Phase IV:* It involves the safety concern of the product, once it has been approved.

Biocompatibility of dental materials

1. *Zinc phosphate cement:* No reported systemic reaction, allergy, or mutagenic/carcinogenic reaction. Locally, it will provoke a stinging reaction for a short period.
2. *Zinc polycarboxylate cement:* No reported systemic reaction, allergy, or mutagenic/carcinogenic reaction. Locally, it produces minimal irritation to the pulp.
3. *Zinc oxide eugenol cement:* No reported systemic reaction, or mutagenic/carcinogenic reaction. It can cause allergic contact dermatitis. Locally, it can produce cytotoxic reaction; eugenol has an obtundent effect when used in deep cavities.
4. *Calcium hydroxide:* No reported systemic reaction, allergy, or mutagenic/carcinogenic reaction. When used as indirect capping material, it exerts antimicrobial activity and decreases the permeability of dentin. In case of direct pulp capping, it produces superficial coagulation necrosis.
5. *Glass ionomer cement:* No reported systemic reaction, allergy, or mutagenic/carcinogenic reaction. Unset cement is cytotoxic to pulp.
6. *Silver amalgam:* No reported mutagenic/carcinogenic reaction. Elemental mercury can lead to systemic toxicity. In deep cavities, it leads to reduced number of odontoblasts, dilated capillaries, and inflammatory cell reaction.
7. *Composite resin:* No reported systemic reaction, mutagenic/carcinogenic reaction. Some components may produce type IV delayed hypersensitivity reaction. It may cause pulpal inflammation.

8. *Ceramics:* No reported local, allergy, or mutagenic/carcinogenic reaction. There is risk of silicosis due to inhalation of ceramic dust.

9. *Dental casting alloys:* No reported systemic reaction. Release of metals may be cytotoxic locally. Lichenoid reactions and allergic reactions have been reported in the oral mucosa. Some components are mutagenic as well as carcinogenic also.

10. *Wrought alloys:* Release of manganese can lead to nervous and skeletal disorders. Corrosion products may cause local pain and swelling. Lichenoid reaction may be seen in oral mucosa. Nickel is a weak mutagen.

11. *Denture base resins:* No reported systemic reaction, or mutagenic/carcinogenic reaction. Chemically activated resin is most cytotoxic. Resins may cause severe pulpal reactions.

12. *Impression materials:* No allergy, or mutagenic/carcinogenic reaction. Some materials are toxic in high concentration. Polyether is highly cytotoxic. Contact dermatitis reaction may also occur.

13. *Endodontic materials*

a. *Latex materials:* No reported systemic reaction, or mutagenic/carcinogenic reaction. It may result in contact dermatitis and latex allergy.

b. *Obturator material:* No reported systemic reaction, or mutagenic/carcinogenic reaction. Gutta percha is slightly cytotoxic. Allergy to gutta percha is very rare.

c. *Root canal sealers:* No reported systemic reaction. Some may cause cytotoxic and allergic reactions.

Q. 11. What are biomimetic substances?

(RGUHS, Nov. 2011)

Ans. Biomimetic refers to the potential ability of a material to mimic nature.

Examples are proteins such as silk, collagen, keratin, gelatin and fibrinogen; polysaccharides such as cellulose, starch, chitin, alginates, amylase, dextran; polynucleotides such as DNA and RNA. In these, the monomeric units are amino acids, sugars and nucleotides respectively.

Advantages

1. They do not evoke toxic reactions that are often in synthetic materials.
2. They may assist in tissue healing or integration.

Disadvantages

1. They can cause immune reactions.
2. They may be contaminated by bacteria and other infectious pathogens.

3. They are difficult to sterilize.
4. They have the tendency to denature at temperature below their melting point.
5. The cost factor is also a limitation.

Q. 12. Write a short note on mercury and dental amalgam. (RGUHS, Nov. 2013)

Ans. An amalgam is defined as a special type of alloy in which mercury is one of the components. Mercury is able to react with other metals to form a plastic mass, which is packed into the prepared cavity. Dental amalgam is the most widely used filling material for posterior teeth. The alloys before combining with mercury are known as dental amalgam alloys.

Classification

- a. *Based on the copper content:* Low copper and high copper alloys.
- b. *Based on zinc content:* Zinc containing and zinc free alloys.
- c. *Based on the shape of particle:* Lathe cut, spherical and spheroidal alloys.
- d. *Based on number of alloyed metals:* Binary, ternary and quaternary alloys.
- e. *Based on size of alloy:* Microcut and macrocut.

Advantages

1. Reasonably easy to insert.
2. Not much technique sensitive.
3. Manifests anatomic form well.
4. Adequate resistance to fracture.
5. Long service life.
6. Cheaper.

Disadvantage

1. The color does not match tooth structure.
2. More brittle.
3. Chances of corrosion and galvanic action.
4. Chances of marginal breakdown.
5. Do not bond to tooth structure.
6. Risk of mercury toxicity.

Applications

1. As a permanent filling material in class I, II cavities.
2. In combination with retentive pins to restore a crown.
3. For making dies.
4. In retrograde filling materials.
5. As a core material.

Q. 13. Write a short note on mercury hygiene in dental office. (MUHS, May 2012)

Ans.

1. All the staff involved in handling mercury should be well trained in management and hygiene protocol.
2. The clinic should be well ventilated with fresh air circulation and outside exhaust.
3. All excess mercury and amalgam waste should be stored in well sealed containers.
4. Proper disposal system should be followed to avoid environmental pollution.
5. Amalgam scrap/mercury contaminated material should not be subjected to heat sterilization.
6. Spilled mercury is cleaned as soon as possible as it is extremely difficult to clean it from carpets.
7. Vacuum cleaners are not used as they disperse the mercury through exhaust.
8. Skin contact with mercury should be washed with water and soap.
9. The alloy mercury capsules should have tight fitting cap.
10. While removing old fillings, a water spray, mouth mask and suction should be used.
11. The use of ultrasonic amalgam condenser is not recommended.
12. All scrap amalgam should be salvaged and stored in air tight container.
13. Professional clothing should be removed before leaving the workplace.
14. Annual programme for handling toxic materials should be monitored for actual exposure levels.

Q. 14. Discuss in detail the various luting agents used in dentistry. (TNMGR, March 2008)

Ans. Luting/bonding/cementing is the process by which crown, restoration and other devices are attached to tooth structure using an intermediate material called cement.

Types

1. *Temporary (short-term) luting cement:* Zinc oxide-eugenol.
2. *Permanent (long-term) luting cements:* Zinc phosphate cement, glass ionomer cement, resin cement, zinc polycarboxylate cement, reinforced zinc oxide eugenol.

Luting mechanism

1. *Non-adhesive:* Luting cement fills the gap between restoration-tooth, and holds by engaging in small surface irregularities. For example, all luting cements.
2. *Micromechanical bonding:* Surface irregularities are enhanced through air abrasion or acid etching to

provide large irregularities for cement to fill and improve the frictional retention. For example, resin cements.

3. *Molecular bonding*: This results from van der Waals forces and a chemical bond between the cement and the tooth surface. For example, zinc polycarboxylate, glass ionomer.

Q. 15. Write a short note on glass ionomers.

(TNMGR, Aug. 2008; RGUHS, Oct. 2010)

Ans. Glass ionomer cements are adhesive tooth colored anticariogenic restorative materials.

Applications

1. Anterior esthetic restorative material.
2. For eroded areas.
3. As luting agent.
4. As liners and base.
5. For core build up.

Classification

Type I: Luting and bonding cement.

Type II: For restorations.

Type III: Liners and base.

Type IV: Pit and fissure sealants.

Composition

Powder: Silica, alumina, aluminium fluoride, calcium fluoride, sodium fluoride, aluminium phosphate, zirconium oxide, lanthanum, strontium, barium.

Liquid: Polyacrylic acid (50%), itaconic acid, maleic acid, tricarballic acid, tartaric acid, water.

Advantages

1. Chemical adhesion to the tooth structure.
2. Anticariogenic potential.
3. Biocompatibility.
4. Tooth colored restorative material.
5. Good marginal integrity.

Disadvantages

1. Inferior mechanical properties.
2. Poor wear resistance.
3. High moisture sensitivity.
4. Poor esthetics.

Q. 16. Write a short note on fillers in composites.

(RGUHS, Oct. 2010; MUHS, May 2012)

Ans. Addition of fillers particles into the resin matrix significantly improves its properties.

Factors affecting

1. Amount of filler added.
2. Size of particles and its distribution.

3. Index of refraction.

4. Radiopacity.

5. Hardness.

Types of fillers

1. *Quartz fillers*: They are obtained by grinding or milling quartz. They are chemically inert and very hard.
2. *Colloidal silica*: They are obtained by pyrolytic or precipitation process.
3. *Glass/ceramics containing heavy metals*: These fillers provide radiopacity to the restorations, e.g. barium, zirconium, strontium glasses.

Advantages

1. Fillers decrease polymerization shrinkage.
2. Fillers decrease the coefficient of thermal expansion.
3. Less water sorption.
4. Fillers improve the mechanical properties, such as hardness, compressive strength, tensile strength and wear resistance.
5. Heavy metal fillers provide radiopacity.
6. They provide means of controlling various esthetic features such as color, translucency, and fluorescence.

Q. 17. Write a short note on titanium.

(TNMGR, Aug. 2008; April 2013)

Q. Write a short note on titanium-molybdenum alloys.

(RGUHS, May 2011)

Ans. Commercially pure titanium has become one of the materials of choice for dental implant material because:

- a. It has low density (4.5 g/cm³) but high strength.
- b. It has minimal biocorrosion due to its passivating effect.
- c. It is biocompatible.
- d. Titanium has good stiffness (5–10 times higher than bone).

Its alloyed form contains 6% aluminum and 4% vanadium.

Surface coated titanium: The newer implant designs use titanium that is coated with a material that bonds and promotes bone growth (bioactive). The implant is coated with a thin layer of tricalcium phosphate or hydroxyapatite or has been plasma sprayed.

Pure titanium has different crystallographic forms at high and low temperatures. At temperature below 885°C the hexagonal close packed or alpha lattice is stable, whereas at higher temperature the metal rearranges into a body centered cubic or beta crystal. Alpha titanium is not used in orthodontic applications,

since they do not have improved springback characteristics. The beta form of titanium can be stabilized down to room temperature by the addition of elements like molybdenum. Beta titanium alloy in wrought wire form is used for orthodontic applications.

Mechanical properties

1. *Modulus of elasticity*: 71.7×10^3 MPa.
2. *Yield of strength*: 860–1170 MPa.
3. The high ratio of yield strength to modulus produces orthodontic appliances that can undergo large elastic activations.
4. Beta titanium can be highly cold worked. It can be bent into various configurations and has formability comparable to that of austenitic stainless steel.
5. *Welding*: clinically satisfactory joints can be made by electrical resistance welding of beta titanium.
6. *Corrosion resistance*: Both forms have excellent corrosion resistance and environmental stability.

Q. 18. Write a short note on metal-free ceramics.

(RGUHS, Oct. 2010)

Ans. Metal-free ceramics/all ceramic restorations without a metallic core or substructure. This makes them esthetically superior to the metal ceramic restorations. They are:

1. Porcelain jacket crown.
2. Ceramic jacket crown with leucite reinforced core.
3. Cast glass ceramic jacket crown.
4. Injection moulded glass ceramic jacket crown.
5. Ceramic restoration with glass infiltrated aluminous core.
6. Ceramic restoration with CAD-CAM ceramic core.
7. Ceramic restoration with copy milled ceramic core.

Composition: Silica, alumina, calcium oxide, soda, potash, boric oxide, zinc oxide, zirconium oxide.

Q. 19. Write a short note on implant surface characteristics.

(TNMGR, March 2008)

Ans. The dental implant surface should stimulate bone growth around them upon placement. Surface characteristics are classified based on the following:

Roughness

- a. *Smooth*: $<0.5 \mu\text{m}$
- b. *Rough*: $0.5\text{--}3 \mu\text{m}$
 - i. *Minimally rough*: $0.5\text{--}1 \mu\text{m}$
 - ii. *Intermediately rough*: $1\text{--}2 \mu\text{m}$
 - iii. *Rough*: $2\text{--}3 \mu\text{m}$

Texture

- a. *Concave*: By additive treatment like hydroxyapatite (HA) coating and titanium plasma spraying.

- b. *Convex*: By subtractive treatments like etching and blasting.

Roughness: It increases the surface area of implant, also improves the attachment and biochemical interaction with the bone. Various methods to increase the roughness are: Machining, acid etching, sandblasting, anodized surface, titanium spraying, porous sintering, HA plasma spraying, and laser modifications.

Q. 20. Discuss about biomaterials used in implants.

(BFUHS, May 2005)

Ans.

a. Metals

1. Stainless steel.
2. Cobalt-chromium-molybdenum based.
3. Titanium and its alloys.
4. Surface coated titanium.

b. Ceramics

1. Hydroxyl apatite.
2. Bioglass.
3. Aluminum oxide.

c. Polymers and composites.

d. Others: Gold, tantalum, carbon, etc.

Q. 21. Write a short note on gypsum material.

(RGUHS, May 2011)

Ans. Gypsum products are derived from the mineral gypsum, chemically known as calcium sulfate dehydrate.

Applications

1. Study models for oral and maxillofacial structures.
2. Cast and die material.
3. Impression material.
4. Investing material in flasking procedure.
5. Investment material for casting of metallic restorations.
6. For mounting stone models onto articulators.

Types: ADA specification no. 25

Type I: Impression plaster (water/powder ratio = $0.40\text{--}0.75$)

Type II: Model plaster, plaster of paris (water/powder ratio = $0.40\text{--}0.55$).

Type III: Dental stone (water/powder ratio = $0.28\text{--}0.33$).

Type IV: Die stone (high strength and low expansion) (water/powder ratio = $0.22\text{--}0.26$).

Type V: Dental stone (high strength and high expansion) (water/powder ratio = $0.18\text{--}0.22$).

Advantages

1. Good reproducibility.
2. Dimensionally accurate and stable.
3. Inexpensive and easy to use.
4. Good color contrast.

Disadvantages

1. Poor mechanical properties causes fracture of teeth from stone cast.
2. Poor abrasive resistance.
3. Poor compatibility with hydrocolloid impression materials.
4. Poor wetting of rubber impression materials.

Q. 22. Write a short note on inlay wax.*(RGUHS, Nov. 2011)*

Ans. Inlay wax is a specialized dental wax that can be applied onto the prepared cavity or to the dies to form direct or indirect pattern.

Uses: Pattern for inlays, crown and bridges.

Ideal requirements

1. When softened, it should be uniform, without graininess.
2. The color should contrast with the die.
3. The wax should not pull or chip.
4. On burnout, it should completely vaporize.
5. The wax pattern should be rigid and dimensionally stable.

Classification

Type I: Medium wax is used for direct technique.

Type II: Soft wax is used for indirect technique.

Composition: Paraffin wax (base), ceresin, gum dammar, carnauba (modifiers), candellila, and coloring agents.

Q. 23. Write a short note on die material.*(BFUHS, May 2005)*

Ans. Die is a positive replica of a prepared tooth or teeth in a suitable hard substance on which inlays, crowns and other restorations are made.

Types of die materials

- a. *Gypsum:* Type IV, V.
- b. *Metal and metal coated dies:* Electroformed, sprayed metals, amalgam.
- c. *Polymers:* Metal/inorganic filled resins.
- d. *Cements:* Silicophosphate or polyacrylic acid bonded cement.
- e. *Refractory materials:* Investments and divestments.

Ideal properties of die material

1. It should be dimensionally accurate.
2. It should have high abrasion resistance.
3. It should have smooth surface.
4. It should be tough.
5. It should be able to reproduce all the fine details.
6. It should be compatible with all impression materials.
7. It should have color contrast.
8. It should be easy to manipulate.
9. It should be noninjurious to health.
10. It should be economical to use.

Q. 24. Write a short note on phosphate bonded investments.*(TNMGR, March 2008)*

Ans. They are used for casting high fusing alloys and base metal alloys.

According to ADA specification no. 42

Type 1: For inlays, crowns, and other fixed restorations.

Type 2: For partial dentures and other removable restorations.

Composition

- a. *Powder:* Ammonium diacid phosphate (binder), silica (refractory material), magnesium oxide, carbon (modifier).
- b. *Liquid:* Silica solution in water.

Setting reaction: Ammonium diacid phosphate reacts with magnesium oxide to give the investment room temperature strength. At higher temperature, ammonium diacid phosphate reacts with silica to form silicophosphate, which increases the strength at higher temperature.

Q. 25. Write a short note on defective casting.*(BFUHS, May 2007, 2008; TNMGR, Sept. 2010; HP, May 2012)***Q. Write a short note on back pressure porosity.***(MUHS, June 2012)***Ans.**

1. **Distortion:** Usually due to distortion of wax pattern. This can be minimized by manipulating wax at high temperature, investing pattern within one hour after finishing.
2. **Surface roughness:** It can be because of:
 - a. Air bubbles on wax pattern.
 - b. Too rapid heating of investment.
 - c. Higher water powder ratio.
 - d. Prolonged heating.
 - e. Too high or too low casting pressure.
 - f. Foreign body inclusion.

3. **Porosity:** External porosity causes discoloration, whereas internal porosity weakens the restoration.
- Shrink spot/localized shrinkage porosity:** Large irregular voids usually found near the sprue-casting junction, occurs due to incorrect cooling sequence.
 - Suck back porosity:** This is an external void usually seen in the inside of a crown opposite the sprue. A hot spot is created by the hot metal impinging on the mould wall near the sprue.
 - Microporosity:** Fine irregular voids within the casting, occurs when the casting freezes too rapidly.
 - Pin hole porosity:** Tiny voids due to release of incorporated gases during solidification.
 - Gas inclusion porosity:** Large voids, due to dissolved gases.
 - Back pressure porosity:** Porous casting with rounded short margins. It occurs due to inadequate venting of the mould. It can be avoided by using adequate casting force, using investment of adequate porosity, by placing pattern not more than 6–8 mm away from the end of the ring and providing vents in large castings.
 - Casting with gas blow hole:** This occurs due to wax residue in the mould, which yields large volumes of gases.
4. **Incomplete casting:** It may occur due to insufficient use of alloy, when mould is not heated to casting temperature, premature solidification of alloy, blocked sprue, back pressure due to gases and low casting pressure.
5. **Too bright/shiny casting with short and rounded margins:** It occurs due to incomplete elimination of wax.
6. **Small casting:** It occurs when the compensation for shrinkage of alloy has not been done by adequate expansion of mould cavity.
7. **Contamination:** It occurs due to oxidation by overheating, using oxidizing zone of flame, failure to use flux.
8. **Black casting:** It occurs due to release of sulfur when the investment is overheated due to incomplete elimination of wax pattern.

Q. 26. Write a short note on polishing agents used in dentistry. (BFUHS, May 2009)

Ans. Polishing agents have finer particle size and less hard than abrasives. They are used for smoothening roughened surfaces.

- Pure alumina.
- Polishing cakes.

- Pumice.
- Garnet.
- Kieselgurh.
- Tripoli.
- Rouge.
- Tin oxide.
- Chalk.
- Chromic oxide.
- Zirconium silicate.
- Zinc oxide.

Q. 27. Write about calcium hydroxide and mineral trioxide. (BFUHS, Nov. 2006, 2008)

Ans. Calcium hydroxide is commonly employed for direct or indirect pulp capping agents, as low strength base, in apexification of teeth incomplete root formation.

Mechanism of action: The ionic form of calcium acts on tissue and induces the formation of hard tissue and has antibacterial effects.

Composition

- Base paste:** Glycol silicate, calcium sulfate, titanium dioxide, calcium tungstate/barium sulfate.
- Catalyst paste:** Calcium hydroxide, zinc oxide, zinc stearate, ethylene toluene, sulphonamide.
Calcium hydroxide reacts with the salicylate ester to form a chelate. Setting time is 2.5–5.5 minutes.

Classification

- Based on setting time**
 - Fast setting.
 - Controlled setting.
 - Low setting.
 - Non-setting.
- Based on form of availability**
 - Powder to be mixed with different vehicle.
 - Single paste, e.g. endocal.
 - Two-paste system: For example, dycal.

Applications

- Conservative procedure:** Pulp capping (direct/indirect).
- Endodontics**
 - Pulpotomy.
 - Apexification.
 - Management of resorption.
 - Management of traumatized teeth.
 - Intracanal medicament.
 - Endodontic sealer.
- Pediatric dentistry:** As obturation material.

Mineral trioxide aggregate (MTA): It is an excellent alternative to the conventional root canal filling materials.

Composition: Calcium silicate compounds and calcium compounds containing aluminum oxide and bismuth oxide.

Properties

1. *Physical state:* Solid powder.
2. *Specific gravity:* 4–4.5
3. *pH:* 12.5
4. *Solubility:* Slightly soluble in water.
5. *Setting time:* 4 hours.
6. *Compressive strength:* 40–70 MPa.

Types

1. Gray MTA.
2. White MTA.

Advantages

1. Excellent biocompatibility.
2. Activates dentinogenesis and cementogenesis.
3. Hydrophilic.
4. Better sealing of setting.
5. Radiopaque.

Disadvantages

1. Difficult to manipulate.
2. Longer setting time.

Clinical applications

1. Vital pulp therapy.
2. Apexification.
3. Perforations.
4. Root resorption.
5. Retrofilling.
6. Obturating material.
7. Barrier for internal bleaching procedures.

Q. 28. Write about root canal filling materials.

(BFUHS, Oct. 2010)

Ans. Root canal filling materials

- a. *Metals:* Silver points, titanium wires, stainless steel files.
- b. *Plastics:* Gutta percha, resilon.
- c. *Pastes:* Mineral trioxide aggregate (MTA), zinc oxide eugenol (ZOE), calcium hydroxide, iodoform pastes, chlorapercha, eucapercha, biocallex, N2.

Q. 29. Write a short note on NiTi wires.

(BFUHS, May 2011)

Ans. The nickel-titanium alloy (nitinol) wires large elastic deflections or working range and limited formability because of their low stiffness and moderately high strength. This alloy exists in various crystallographic forms. At high temperature, a stable body centered cubic lattice. On appropriate cooling or

an application of stress, this transforms to a close packed hexagonal martensitic lattice with associated volumetric change. This behavior of alloy results in shape memory and super elasticity/pseudoelasticity. The memory effect is achieved by first establishing a shape at temperatures near 482°C. The appliance is then cooled and formed into a second shape. Subsequent heating through a lower transition temperature causes the wire to return to its original shape. The phenomenon of super elasticity is produced by transition of austenite to martensite by stress due to volume change which results from the change in crystal lattice. Unloading results in the reverse transition and recovery. This characteristic is useful in some orthodontic situations because it results in low forces and a very large working range or springback.

Composition

Nickel: 54%

Titanium: 44%

Cobalt: 2%

Properties

1. *Shape memory:* It refers to the ability of the material to remember its original shape after being plastically deformed while in the martensitic form.
2. *Superelasticity/pseudoelasticity:* This is stress induced change in the form from austenitic to martensitic form, which gets reversed on the removal of the stress.

Types of NiTi alloys

1. Martensitic stabilized alloys.
2. Austenite active alloy.
3. Martensite active alloy.

Advantages

1. Excellent resiliency.
2. Good springback property.
3. Low load deflection rate.
4. Exert very low forces.

Disadvantages

1. Lack of formability.
2. Loops for closing spaces or bends for opening bites cannot be placed.
3. Wires can easily move in the mouth and can cause trauma to mucosa.
4. Brittleness.
5. High cost.

Clinical uses

1. Ideal for use in initial alignment stage.
2. They can be used as an early leveling and alignment wires.

3. They can be used to make NiTi palatal expanders, coil springs and separators.
4. As actuators.
5. As robotics.

Q. 30. Write a short note on stainless steel and nitinol.
(TNMGR, April 2012)

Ans. Steel is an iron-based alloy which contains less than 1.2% carbon. When chromium (12–30%) is added to steel, the alloy is called as stainless steel. Elements other than iron, carbon and chromium may also be present, resulting in a wide variation in composition and properties of the stainless steels. These are resistant to tarnish and corrosion, because of the passivating effect of the chromium. A thin, transparent but tough and impervious oxide layer forms on the surface of the alloy when it is exposed to air, which protects it against tarnish and corrosion. It loses its protection if the oxide layer is ruptured by mechanical or chemical factors.

Types: Based upon the lattice arrangement of iron:

1. *Ferritic stainless steel:* Body centered cubic structure.
2. *Martensitic stainless steel:* Body centered tetragonal structure.
3. *Austenitic stainless steel (18–8 stainless steel):* Face centered cubic.

Sensitization: It is loss resistance to corrosion of stainless steel if it is heated between 400 and 900°C. It occurs because of precipitation of chromium carbide at the grain boundaries at high temperatures.

Stabilization: This is used to minimize the sensitization. In this method some metal elements are introduced that precipitates as carbide in preference to chromium. For example, titanium.

Q. 31. Write a short note on allergy due to nickel alloy.
(RGUHS, May 2011)

Ans. Nickel is the most common component of the super-elastic nickel-titanium (NiTi) archwires used during the initial leveling and aligning phase of orthodontic treatment. Nickel is known allergen, more so in females than males. It results in contact dermatitis and hypersensitivity. OSHA regulations allow 15 µg/m³ of nickel in air.

Immune response: The response by the immune system to nickel is usually a Type IV cell-mediated delayed hypersensitivity also called an allergic contact dermatitis. It is mediated by T cells and monocytes/macrophages.

Diagnosis: The diagnosis of a response to nickel in the oral mucosa is more difficult than on the skin. A

diagnosis can be confirmed by conducting a cutaneous sensitivity test called a patch test using 5% nickel in petroleum jelly. Oral clinical signs and symptoms of nickel allergy can include the following: A burning sensation, gingival hyperplasia, labial desquamation, angular cheilitis, erythema multiforme, periodontitis, stomatitis with mild to severe erythema, papular perioral rash, loss of taste or metallic taste, numbness, soreness at side of the tongue.

Treatment

1. The nickel titanium archwire should be removed and replaced with a stainless steel archwire which is low in nickel content or preferably a titanium-molybdenum alloy (TMA), which does not contain nickel.
2. Resin coated NiTi wires are also an option. These resin-coated wires have had their surface treated with nitrogen ions, which forms an amorphous surface layer. Manufacturers claim that this results in an increase in corrosion resistance and decreased amount of leaching of nickel, more so than both Ni-Ti and stainless steel wires.
3. If any severe allergic reaction develops, the patient should be referred to a physician to be treated with antihistamines, anesthetics or topical corticosteroids.

Q. 32. Write a short note on biomaterials used for alveolar ridge augmentation. (TNMGR, April 2013)

Ans.

a. Bone replacement grafts

1. *Autogenous bone grafts/autografts:* From same individual. Intraoral from mandibular symphysis, maxillary tuberosity, ramus, exostosis. Extraoral from iliac crest, tibial plateau.
2. *Allografts:* From a genetically dissimilar member of the same species. For example, mineralized or demineralized freeze dried bone allografts.
3. *Xenografts/heterografts:* From donor of another species. For example, bovine.
4. *Isograft:* It refers to a graft between genetically identical individuals.
5. *Alloplasts:* Natural or synthetic materials. For example, ceramic materials, synthetic calcium phosphate ceramics, calcium carbonate, HTR polymers, bioactive glass ceramics.

b. Membranes used in guided tissue and bone regeneration

1. *Non-resorbable membranes:* Cellulose filters, expanded polytetrafluoroethylene membrane (e-PTFE), dental rubber dam, titanium membranes.
2. *Resorbable membrane:* Collagen membranes, PLA/PGA, synthetic liquid polymer, polyglactin, calcium sulfate.

Q. 1. Write about principle of orofacial genetics.

Ans. Genetics is concerned with the inheritance of traits (normal or abnormal), and interaction of genes and the environment. Genotype is genetic constitution of an individual. Phenotype is observable characteristic of the individual. The proportion of phenotypic variance attributable to the genotype is known as heritability.

1. In specific traits, individual genotypes are readily identified and differences are qualitative. For example, ABO blood.
2. In continuous traits, difference is characterized quantitatively between individuals. For example, height, weight, tooth size.
3. The quantitative traits are modified by environmental factors.
4. The genetic variation may be dependent on segregation of multiple genes, polygenes.
5. The genetic difference caused by polygene is known as polygenic variation.
6. Different types of genetic product are being considered as different distances from the fundamental level of gene activity. For example, enzymes and its genetic variants.
7. Morphological characters are the end result of vast complexity of interacting, hierarchical, biochemical and developmental process.
8. Each gene influences many morphological characters (pleiotropic), so that a deleterious mutation results in a syndrome.
9. Each morphological character may be dependent on many different genes.

Modes of inheritance (KUHS, June 2013; RUHS, May 2015):

The different ways in which genes are handed down from parents to offspring's and expresses them.

1. *Autosomal dominant*: When one member of the allelic pair is able to express itself irrespective of the pre-

sence of other member. For example, dentinogenesis imperfecta, amelogenesis imperfecta, achondroplasia.

2. *Autosomal recessive*: Inheritance depends on the expression of both the members of the allelic pair. For example, cystic fibrosis, hypophosphatasia.
3. *Sex-linked*: These traits carried by genes present on sex chromosomes X and Y. For example, ectodermal dysplasia, hemophilia.
4. *Co-dominant*: When both members of the chromosomes pair are able to express themselves fully in the phenotype. For example, ABO blood group.
5. *Intermediate*: When a trait is expressed as a result of partial expression of both chromosomes of a pair. For example, sickle cell trait.
6. *Monogenic*: These traits are produced and regulated by a single gene locus. For example, albinism, neurofibromatosis.
7. *Polygenic*: Multiple genes control the trait, e.g. height of an individual.
8. *Multifactorial*: These traits are determined by the interaction of multiple genes and environmental factors. For example, cleft lip and palate.

Q. 2. Write a short note on twin studies.

(RGUHS, May 2013)

Ans. Twin studies have been a valuable source of information about the genetic basis of complex traits. To maximize the potential of twin studies, large, worldwide registers of data on twins and their relatives have been established. Twin studies can be used to obtain insights into the genetic epidemiology of complex traits and diseases, to study the interaction of genotype with sex, age and lifestyle factors, and to study the causes of co-morbidity between traits and diseases. By facilitating comparisons between monozygotic (MZ) and dizygotic (DZ) twins, twin registers represent some of the best resources for evaluating the importance of genetic variation in susceptibility to disease.

Classification

1. **Classical MZ-DZ comparison:** These studies estimate the contributions of genetic and environmental effects to phenotypic variance, and test, e.g. for age, cohort and sex differences in gene expression.
2. **Multivariate analyses (simultaneous analysis of correlated traits):** This involves direction of phenotypic causality, causes of co-morbidity of two or more traits, multivariate modeling of environmental and genetic correlations between traits.
3. **Co-twin control study:** Case control studies of MZ twins who are perfectly matched for genes and family background; also used to study gene expression in discordant twins.
4. **Extended twin study (studies of twins and their families):** In this study parents can be included to study cultural transmission, to determine genetic and environmental stability; social interactions and special twin effects. Also maternal effects and imprinting can be studied if offspring of MZ twins are included.
5. **Genotyping at candidate loci:** These include genotyping of MZ twins to detect variability genes and penetrance; genotyping of DZ twins to estimate associations within and between families.
6. **Genotyping at marker loci:** These include genotyping of DZ twins to detect linkage with quantitative trait loci; selecting informative families from large twin registers.

Q. 3. Write a short note on single gene disorders.

(KUHS, Jan. 2014)

Ans.

Classification

a. Autosomal disorders

1. **Autosomal dominant disorders:** Arise due to defect in at least one gene out of pair of genes on autosomes.

Features

- a. Disease appears in each generation.
- b. Delayed age of onset.
- c. Vertically transmitted.
- d. Affected individual has an affected parent.
- e. Male and female are equally affected.
- f. Capability of transmission is same in both the parents.
- g. Each child is at 50% risk of inheriting the abnormal gene.

Examples: Osteogenesis imperfecta, mesiodens, dentinogenesis imperfecta, dentin dysplasia, Apert's syndrome.

2. **Autosomal recessive disorders:** Occur when both the genes on autosome are affected. Since two abnormal genes are required for obtaining a given clinical phenotype and their incidence is low compared to autosomal dominant disorders.

Features

- a. Sudden onset of illness.
- b. Male and female are equally affected.
- c. Early age of onset.
- d. Consanguinity increases the incidence.
- e. Most of the offsprings are normal.
- f. Affected individual may or may not have affected parent.

Examples: Dentin dysplasia (coronal type), amelogenesis imperfecta (hypocalcified II), hypophosphatasia, Hurler's syndrome.

b. X-linked disorders

1. **X-linked dominant disorders:** Arises from an affected heterozygote female.

Features

- a. Both sexes are affected, male > female.
- b. Absence of father to son transmission.
- c. All the female of affected father are affected.
- d. Affected females have deficiency of live born sons.

Examples: Vitamin D resistant rickets, orofacial digital syndrome.

2. **X-linked recessive disorders:** Arise in female recessive homozygotes or less commonly male hemizygotes.

Features

- a. Males are mostly affected.
- b. Complete absence of male to male transmission.
- c. Female carrier has a 25% chance of having affected son.
- d. Each child of affected parents is at 50% risk of transmission.

Examples: Hemophilia, Fabry disease.

Q. 4. Write about craniofacial anomalies.

Ans. Craniofacial anomalies are a diverse group of deformities in the growth of head and facial bones. These are congenital and may vary in severity.

1. Cleft lip and/or palate: Most common congenital craniofacial anomalies seen at birth.
2. Cleft lip.
3. Cleft palate.
4. Craniosynostosis—crouzon syndrome, Apert syndrome.

5. Hemifacial microsomia (Goldenhar syndrome, brachial arch syndrome, facioauriculovertebral syndrome, oculoauriculovertebral spectrum, or lateral facial dysplasia).
6. Vascular malformation—hemangioma, lymphangioma.
7. Deformational or positional plagiocephaly—holoprosencephaly, Stickler syndrome.

Q. 5. Write a short note on chromosomal aberrations.

Ans.

a. Structural aberrations

1. Deletion—Turner's syndrome.
2. Ring chromosome.
3. Inversion.
4. Duplication.
5. *Translocation*: Philadelphia chromosome seen in CML.

b. Numerical aberrations

1. *Autosomal*: Down's syndrome (trisomy 21), Edward syndrome (trisomy 18), Patau syndrome (Trisomy 13).
2. *Sex chromosomal*: Turner's syndrome, superfemale, Klinefelter's syndrome.

Q. 6. Write a short note on mutations.

(TNMGR, March 2010)

Ans. A mutation is a sudden, permanent inheritable change in the genetic material. The mutation may be due to the insertion or deletion of a nucleotide, the substitution of one nucleotide with another or inversion of two nucleotides.

1. A 'nonsense' mutation changes an amino acid specifying codon into a chain terminating codon.
2. 'Frame shift' is a mutation arising from the insertion or deletion of one or more nucleotides that causes gene to be misread during translation into the polypeptide.

Causes of mutation

1. *Spontaneous mutations*: Result from errors in replication of DNA, due to enzyme defect.
2. *Induces mutations*: Changes in the DNA caused by the effects of mutagens. Examples are:
 - i. *Ionising radiations*: X-rays, cosmic rays, etc.
 - ii. *Non-ionising radiations*: UV rays.
 - iii. *Chemicals*: Mustard gas.

Q. 7. Write about genetic basis of dental caries.

(RGUHS, May 2011)

Ans.

1. Variation in caries risk and protection has a strong genetic component.

2. Traits such as tooth morphology, immune response saliva, and diet contribute the genetic determination of dental caries.
3. Only a few specific genes are associated with caries risk, e.g. amelogenin, ameloblastin and tuftelin.
4. Variation in genetics also influences the difference in dietary habits that influence the caries risk.
5. The genes associated with enamel formation, taste, saliva contribute to caries risk and/or protection.
6. Fluoride and other environmental factors can override this genetic influence.
7. An association has been found between caries experience and the proline-rich protein in saliva.
8. The inheritance of proline-rich proteins follows an autosomal dominant mode.

Q. 8. Write about genetic basis of malocclusion.

(TNMGR, March 2010)

Ans. Genetics and environmental factors play an important role in etiology of malocclusion.

1. **Class II division 1**: Studies have shown a higher correlation between the patients and his immediate family and data from random pairings of unrelated siblings, thus supporting the concept of polygenic inheritance for class II division 1 malocclusion.
2. **Class II division 2**: Family occurrence has been reported in twin and triplet studies and in family pedigrees.
3. **Class III malocclusion**: Family studies of mandibular prognathism are suggestive of heredity in the etiology of this condition.
4. **Population differences**: Growth records of Aborigines have shown that a fairly large percentage of variations observed in tooth size are due to genetic factors. Certain teeth show more variability in size, shape and eruption. For example, third molars.

Q. 9. Describe in detail the various congenital anomalies causing malocclusion.

(TNMGR, Oct. 2013)

Ans. Many congenital malformations involve malocclusion of the teeth.

1. Clefts of the lip and palate.
2. Hemifacial microsomia.
3. Mandibulofacial dysostosis.
4. Robin complex.
5. Nager acrofacial dysostosis.
6. Wilder Vanck-Smith syndrome.
7. Hallermann-Streiff syndrome.
8. Basal cell nevus syndrome (Gorlin-Goltz syndrome).
9. Klinefelter syndrome.
10. Marfan syndrome.
11. Crouzan's syndrome

Q. 10. Write a short note on gingival lesion of genetic origin. (TNMGR, Oct. 2012)

Ans. These are following diseases of genetic origin, which manifest as gingival lesion:

1. Ehlers-Danlos syndrome.
2. Familial fibromatoses.
3. Neurofibromatosis 1.
4. Acatasia.
5. Hypophosphatasia.
6. Papillon-Lefevre syndrome.
7. Down's syndrome.
8. Leukocyte adhesion defect.
9. Cyclic neutropenia.
10. Chédiak-Higashi syndrome.

Q. 11. Write a short note on genetic polymorphism. (TNMGR, Sept. 2009)

Ans. Most human diseases have a genetic component to the etiology. Genetic diseases have been broadly classified into two groups: Simple mendelian diseases and complex diseases.

1. **Simple mendelian diseases (monogenic disorders):** These are caused by a mutation in a single gene and are referred to as single gene (major gene effect) disorders. Inheritance patterns are autosomal dominant or of the autosomal recessive type.
2. **Complex genetic diseases (polygenic disorders):** They are a result of the interaction of multiple different gene loci, environmental, and behavioral factors. Many of the diagnostic features of these complex diseases also called quantitative trait disorders are regulated by several genes. Complex diseases are associated with variations in multiple genes, each having a small overall contribution and relative risk for the disease process. The clinical condition may not be evident unless two different genetic factors are present.

Polymorphisms and mutations: A major difference in the genetic basis for simple mendelian diseases and complex genetic diseases is the number of genes involved, and the contribution of each gene to the overall disease phenotype. The fact that the genetic alteration is predictably associated with a disease phenotype indicates that there is no redundancy or compensation in the particular biological system that can overcome the effect of the underlying genetic defect. Such a genetic alteration is termed 'mutation' as in the case of mendelian diseases. The genetic alterations that contribute to complex diseases are individually of much smaller effect and are generally called 'generally polymorphisms' because they are

prevalent in the population. When a specific allele occurs, in at least 1% of the population, it is said to be genetic polymorphism. In contrast to mutations that have been casually linked with mendelian diseases, genetic polymorphisms are often not directly casually linked, but rather specific alleles are reported to be found more frequently in diseased individuals than in non-affected controls.

Examples are: Cytokine gene polymorphisms, receptor gene polymorphisms, antigen-antibody gene polymorphisms, polymorphisms in genes encoding enzymes.

Q. 12. Write a short note on genetic engineering.

(BFUHS, Oct. 2010)

Ans. Genetic engineering, also called genetic modification is a set of technologies used to change the genetic makeup of cells, including the transfer of genes within and across species boundaries to produce improved or novel organisms. New DNA may be inserted in the host genome by first isolating and copying the genetic material of interest using molecular cloning methods to generate a DNA sequence, or by synthesizing the DNA, and then inserting this construct into the host organism. Genes may be removed, or "knocked out", using a nuclease. An organism that is generated through genetic engineering is considered to be a genetically modified organism (GMO).

If genetic material from another species is added to the host, the resulting organism is called transgenic. If genetic material from the same species or a species that can naturally breed with the host is used the resulting organism is called cisgenic. Genetic engineering can also be used to remove genetic material from the target organism, creating a gene knockout organism.

Genome editing: Genome editing is a type of genetic engineering in which DNA is inserted, replaced, or removed from a genome using artificially engineered nucleases, or "molecular scissors." The nucleases create specific double-stranded breaks (DSBs) at desired locations in the genome, and harness the cell's endogenous mechanisms to repair the induced break by natural processes of homologous recombination (HR) and nonhomologous end-joining (NHEJ). There are currently four families of engineered nucleases: Meganucleases, zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and the Cas9-guideRNA system.

Applications: Genetic engineering has applications in medicine, research, industry and agriculture and can be used on a wide range of plants, animals and micro-organisms.

Medicine: In medicine, genetic engineering has been used in manufacturing drugs, to create model animals and do laboratory research, and in gene therapy.

Manufacturing: Genetic engineering is used to mass-produce insulin, human growth hormones, human albumin, monoclonal antibodies, antihemophilic factors, vaccines and many other drugs. Genetically engineered viruses are being developed that can still confer immunity, but lack the infectious sequences.

Research: Genetic engineering is used to create animal models of human diseases. Genetically modified mice are the most common genetically engineered animal model. They have been used to study and model cancer, obesity, heart disease, diabetes, arthritis, substance abuse, anxiety, aging and Parkinson disease. Potential cures can be tested against these mouse models. Also genetically modified pigs have been bred with the aim of increasing the success of pig to human organ transplantation.

Gene therapy: Gene therapy is the genetic engineering of humans, generally by replacing defective genes with effective ones. This can occur in somatic tissue or germline tissue.

Q. 13. Write a short note on gene therapy.

Ans. Gene therapy is the replacement of person's faulty genetic material with normal genetic material to treat or cure a disease or abnormal medical condition (US Food and Drug Administration).

Faulty genes can be corrected by several methods

1. Regulation of particular gene (the degree to which the gene is turned on or off) can be changed.
2. Faulty gene can be replaced for a normal gene through homologous recombination.
3. Normal gene is inserted into nonspecific location within the genome to replace a nonfunctional gene.
4. Abnormal gene is repaired through selective reverse mutation.

General principles of gene transfer: The concept of gene therapy involves the introduction of exogenous genes into somatic cells that form the organs of the body to produce a desired therapeutic effect. The selected DNA fragment is first cleaved using restriction endonucleases. Then vector or vehicle is prepared to transfer the genetic material. The vector is isolated, purified and cleaved to allow insertion of the DNA fragment. The DNA fragments then must be joined to the cleaved ends of the vector, effectively closing the molecule. This successful insertion of an exogenous DNA molecule into a vector results in a DNA chimera. These vector

constructs are the basis of recombinant DNA techniques. Next step involves introduction of the construct into a cell, allowing the production of a line of genetically identical cells containing the DNA sequence introduced by the vector. This allows mass production of cells with a specifically designed genetic make-up. Vector delivers the therapeutic gene into patient's target. The target cells become infective with therapeutic gene through vector. Functional proteins are created from the therapeutic gene causing the cell to return to a normal stage.

Requirements for vector: The ideal requirements for vectors are:

1. It should not be identified by immune system (non-immunologic).
2. Should be stable and easy to reproduce.
3. Should have longevity of expression.
4. Should have high efficiency (100% cells transfected).
5. High specificity and low toxicity.
6. It should be able to protect and deliver DNA across the cell membrane into the nucleus. It should be able to target gene delivery to specific cells.
7. It should be easy to be produced in large amounts and be inexpensive.

Types of Vector for Gene Therapy

- a. Viral vectors:** Commonly used viral vectors are adenovirus; adeno associated virus (AAV), retrovirus and herpes simplex virus.
- b. Nonviral vectors:** Gene transfer mediated by non viral vectors is referred to as transfection.
 1. *Physical vectors:* Electrophoration, microinjection and use of ballistic particles.
 2. *Chemical vectors:* Include calcium vectors, lipids and protein complexes.

Nonviral methods present certain advantages over viral methods, with simple large scale production and low host immunogenicity.

Types of Gene Therapy

1. **Germline gene therapy:** Repair or replace defective gene in germline cell. Modified gene would be inherited.
2. **Somatic gene therapy:** Repair or replace defective gene in some or all body cells of an individual. But the change is not passed to next generation.

Types of Delivery

1. **In vivo:** Delivery of gene takes place in the body. During *in vivo* gene transfer, the foreign gene is injected into the patient by viral and nonviral methods.

2. **Ex vivo:** Delivery takes place outside the body and the cells are placed back into the body. *Ex vivo* gene transfer involves a foreign gene transduced into tissue cells cultivated in laboratory outside the body, and then resulting genetically modified cells are transplanted back into the patient.

Successful gene therapy requires that

1. Genetic nature of the disease is completely understood.
2. Genes can be delivered to the target cells of affected tissue/organ.
3. Transfected gene should be active for intended duration.
4. Harmful side effects if seen should be manageable.

Difficulties in gene therapy include

1. Difficulty to deliver genes in some sites like lung cells.
2. Genes might integrate at sites where it can affect the functioning of another gene.
3. Vectors may be recognized as foreign by immune system triggering immune response.
4. Viral vector may cause toxicity, inflammatory response and might recover their ability to cause disease.
5. Multigene disorders are difficult to treat by gene therapy.
6. Gene therapy is expensive

Applications in Dentistry

1. **Bone repair:** Bone morphogenic protein (BMPs 2, 4 and 7) are the only growth factors which can singly induce *de novo* bone formation both *in vitro* and at heterotopic sites. Bone defects in the oral and maxillofacial region can be repaired by transferring genes encoding BMPs. The advantage of an *ex vivo* gene transfer approach is that specific cells like bone marrow cells or stem cells can be selected as the cellular delivery vehicle for specific clinical problems. In addition, *ex vivo* strategies have a high efficiency of cell transduction.
2. **Pain:** The use of gene transfer technology offers a potentially novel approach to manipulate specific, localized biochemical pathways involved in pain generation. The use of gene transfer in place of drug delivery to achieve the continuous release of short-lived bioactive peptides in or near the spinal dorsal horn underlies the most common strategies for gene therapy of pain. Also direct gene delivery to the articular surface of the temporomandibular joint has been found to be feasible.

3. **DNA vaccination:** DNA vaccination will play a role in future strategies for preventing periodontal diseases and dental caries. Immunization of salivary gland using plasmid DNA encoding the *Porphyromonas gingivalis* fimbrial gene leads to the production of fimbrial protein locally in the salivary gland tissue with consequent production of specific salivary immunoglobulin A, or IgA, and immunoglobulin G, or IgG, antibodies and serum IgG antibodies. Also generation of antigen specific cytotoxic T lymphocytes can be achieved resulting in protection from *P. gingivalis*. Also any secreted fimbrial protein in saliva could bind to pellicle components and also inhibit the attachment of *P. gingivalis* to the developing plaque.

4. **Keratinocyte:** Presence of stem cells in keratinocytes is also an advantage. They are easily accessible and so monitoring can be accurate. Cultured oral keratinocytes have been grafted to oral surgical defects. They persist at these sites and exhibit normal epithelial morphology. Human growth hormone, apolipoprotein E and the coagulation cascade factor IX are successfully delivered by genetically modified keratinocytes. Gene therapy can be used to treat keratinocytes disorders and dermatologic disorders like ichthyosis and epidermolysis bullosa.

5. **Salivary glands:** Salivary glands produce large amount of proteins and are sites easily accessible for gene transfer with minimum invasiveness through intraductal cannulation. The opening of the main duct in the oral cavity is cannulated and gene delivery vectors, viral or nonviral, are infused by a retrograde injection. Aim is to provide gene therapy to patients suffering from irreversible salivary gland dysfunction resulting from either irradiation for head and neck cancers or the autoimmune damage occurring with Sjögren's syndrome by augmenting salivary secretions by transferring genes that encode secretory proteins into salivary glands. The proteins are subsequently secreted in an exocrine manner.

6. **Oral cancer:** The general strategy in cancer treatment is to express a gene product that will result in cancer cell death. It can be achieved by:
 - a. Addition of a tumor-suppressor gene (gene addition therapy).
 - b. Deletion of a defective tumor gene (gene excision therapy).
 - c. Down-regulation of the expression of genes that stimulate tumor growth.
 - d. Enhancement of immune surveillance (immunotherapy).

- e. Activation of prodrugs that have a chemotherapeutic effect and cause toxicity only to tumor cells ("suicide" gene therapy).
- f. Introduction of genes to inhibit tumor angiogenesis.
- g. "Cancer vaccination" with genes for tumor antigens.

The goal of gene therapy in cancer is to introduce new genetic material into cancer cells that will selectively kill the cancerous cells, causing no toxicity to surrounding normal cells. Vectors such as adenoviruses are useful for gene therapy of head and neck cancers. Replacing a mutated p53 gene with a wild-type (normal) p53 gene is a potential approach to head and neck cancer treatment. Inactivation of p16 is believed to be one of the first steps in head and neck cancer carcinogenesis, and may therefore be an ideal target for gene replacement therapy. Gene transfer of gene p27 was found to inhibit the cell cycle of tumor cells, inducing apoptosis and triggering the suppression of tumor growth. The tumor suppressor genes p16, p21, p27, and Rb are frequently mutated in head and neck cancer, and therefore are potential gene therapy targets. A novel method is gene-directed enzyme-prodrug therapy. In this a recombinant virus is generated which encodes a prodrug-activating enzyme such as nitroreductase, thymidine kinase or cytosine deaminase. Once delivered to the tumor cell, the enzyme is able to convert a harmless prodrug (administered locally or systemically) into a highly toxic cytotoxic drug. The activated drug is able to leech out of the virus-infected cell to kill surrounding non-infected cells, creating a bystander effect in cancer. Increasing the sensitivity of the tumor to normal therapeutic processes by suppressing NF- κ B activity with the use of gene therapy is also a good approach.

7. **Orthodontic tooth movement:** Tooth movement depends on the remodeling of alveolar bone, which is controlled by osteoclasts and osteoblasts. Gene therapy with osteoprotegerin (OPG) and RANKL has been used to inhibit and accelerate orthodontic tooth movement in a rat model. Local RANKL gene transfer to the periodontal tissue accelerated orthodontic tooth movement by approximately 150% after 21 days, without eliciting any systemic effects. Thus, it can be helpful for shortening orthodontic treatment and also for moving ankylosed teeth. Local OPG gene transfer inhibited tooth movement by about 50% after 21 days of forced application.
8. **Gene therapy to grow new teeth:** This approach is generally presented in terms of adding molecules to

induce *de novo* tooth initiation in the mouth. It might be combined with gene-manipulated tooth regeneration. The Baylor College of Medicine has found PAX 9, a master gene critical for tooth development. *de novo* repression or activation of genes such as RUNX2 or USAG-1 might be used to stimulate the third dentition in order to induce new tooth formation in the mouse.

Q. 14. Write a short note on gene mapping.

Ans. Gene mapping refers to the mapping of genes to specific locations on chromosomes. It is a critical step in the understanding of genetic diseases. There are two types of gene mapping:

1. **Genetic mapping:** Using linkage analysis to determine the relative position between two genes on a chromosome.
2. **Physical mapping:** Using all available techniques or information to determine the absolute position of a gene on a chromosome.

Genetic marker requires informative markers—polymorphic and a population with known relationships. It is best if measured between "close" markers.

Unit of distance in genetic maps = centiMorgans (cM).

1 cM = 1% chance of recombination between markers.

Physical mapping relies upon observable experimental outcomes:

1. Hybridization.
2. Amplification.

It may or may not have a distance measure.

The ultimate goal of gene mapping is to clone genes, especially disease genes. Once a gene is cloned, we can determine its DNA sequence and study its protein product.

For example, cystic fibrosis (CF) (P249). In 1985, the gene was mapped to chromosome 7q31–q32 by linkage analysis. Four years later, it was cloned by Francis Collins and his co-workers.

Gene maps

1. Genetic map.
2. Physical map.
3. Transcription map.
4. Sequence map.

Techniques of gene mapping

1. **Gene mapping by in situ hybridization:** The method which involves hybridizing labeled DNA (or RNA) probes directly to metaphase chromosomes.

2. *Gene mapping by somatic cell hybridization*: In this cells from two different species (e.g. humans and rodents) are artificially fused together. These culture lines are developed by mixing human and mouse cells in the presence of the Sendai virus. The virus facilitates the fusing of the two cell types to form a hybrid cell. Human chromosomes are randomly lost from the hybrid cell lines; a few human chromosomes are retained. Because the human and mouse chromosomes can be distinguished by chromosome staining techniques, it can be determined which human cells are retained with a specific cell line.
3. *Gene mapping by gene dosage using patient cells*: The method which to detect dosage differences in either gene products or gene sequences themselves between patient's cell lines containing different numbers of copies of a particular gene. The gene dosage strategy was originally used to assign genes to chromosome 21 by detecting levels of enzyme activity in cell lines from patients with Down syndrome that were 1.5-fold higher than levels in cell lines from chromosomally normal persons, i.e. gene for SOD (superoxide dismutase). At the DNA level, the dosage approach has been used increasingly to assign DNA markers to the X chromosome.
4. *Gene mapping by chromosomal aberration*: To detect directly chromosomal aberration involving genes this may lead to particular disease. Example, Duchenne muscular dystrophy (DMD), X-linked recessive inheritance, is very rare in female. Karyotype analysis of several affected female indicated common X-A translocation. Although these translocations involved different autosomes, their broken points on X chromosomes were commonly located on Xp21. This indicated that the broken points were inner of the gene for DMD.
5. *Gene mapping by linkage analysis*: Linkage analysis is a method of mapping genes that uses family studies to determine whether two genes show linkage when passed on from one generation to the next. Linkage analysis is a tremendously important and powerful approach in medical genetics because it is the only method that allows mapping of genes, including disease genes that are detectable only as phenotypic traits.

Q. 15. Write a short note genetic markers.

(RGUHS, Sept. 2006)

Ans. A genetic marker is a DNA sequence that is readily detected and whose inheritance can easily be monitored. They are used to flag the position of a particular characteristic.

1. **Non-PCR based**: Restriction fragment length polymorphism RFLP.

2. **PCR based**

- a. **RAPD**: Random amplification of polymorphic DNA.
- b. **AFLP**: Amplified fragment length polymorphism.
- c. **SCAR**: Sequence characterize amplified region.
- d. **STS**: Sequence tagged sites.
- e. **EST**: Express sequence tags.
- f. **SNP**: Single nucleotide polymorphism.
- g. **SSR**: Simple sequence repeats.
- h. **CAPS**: Cleaved amplified polymorphic sequence.

Properties of ideal genetic marker

1. It must be polymorphic.
2. Co-dominant inheritance.
3. It should be evenly and frequently distributed throughout the genome.
4. It should be easy, fast and cheap to detect.
5. It should be reproducible.
6. It has high exchange of data between laboratories.

Applications

1. Measure of genetic diversity.
2. Finger printing.
3. Genotypic selection.
4. Genotyping pyramiding and introgression.
5. Indirect selection using quantitative traits loci.
6. Marker assisted selection.
7. Identification of genotype.
8. In genetic maps.

Q.16. Write a short note on genetic counseling.

(TNMGR, Sept. 2010)

Ans. Genetic counseling is a communication process in which individuals seeking advice are provided with all the scientific informations to enable them in making a decision about current or future pregnancies. Procedures for prenatal diagnosis:

1. **Visualization of fetus**

Ultrasonography: With this technique it is now possible to visualize the embryo as early as 5½ to 6 weeks of pregnancy and cardiac activity is detectable at 7–8 weeks. Ultrasonography has now become a routine procedure for verification of viable embryo, determination of gestational age, diagnosis of multiple gestation, determination placental and fetal position, diagnosis of fetal anomalies, detection of uterine malformation and guide for passage of instrument for invasive procedures.

Radiography: Although mineralization of fetal skeleton at 11 weeks of gestation is adequate to permit radiographic examination. This procedure has been discarded due to safety reasons.

Fetoscopy: It has been employed for cannulation of umbilical vessels and for blood sampling transfusion and fetal tissue biopsies.

2. Analysis of fetal tissue

Amniocentesis (optimum time: 16–18 weeks of gestation). Under strict aseptic conditions and local anesthesia, 20–30 ml of fluid is aspirated. The fibroblast-like cells obtained at amniocentesis can be cultured in a variety of tissue culture media enriched with fetal bovine serum for 1–3 weeks permitting accumulation of sufficient dividing cells for karyotyping. A minimum of 15 cells are examined and the modal chromosome number is established. Sex determination of fetus is 99% accurate by this method.

Chorionic villus sampling (CVS): The chorion contains the mitotically active villus cells, and is therefore, the area to be biopsied. At 9–12 weeks of gestational age villi float freely within the intervillous space and are attached only loosely to the underlying structure. In CVS sampling 10–25 mg of chorionic villi is collected. Because the Langerhans' cells of the cytotrophoblast are in dividing phase, it is possible to perform a "direct" chromosome analysis, immediately after sampling, or alternately after 24 hours of incubation in a tissue culture medium. Direct analysis has the great advantage of permitting a fetal chromosome analysis within 24–48 hours.

Fetal and maternal blood analysis: Isolation and analysis of fetal cells in maternal blood is an attractive method of non-invasive prenatal diagnosis. Flow cytometric test of maternal blood with anti-gamma globin MAb (monoclonal antibody to gamma chain of hemoglobin molecule) is highly specific for examining fetal cells with respect to its gender because the amount of gamma hemoglobin chain produced per cell is significantly higher in fetus in comparison to that of adults. With the development of cell sorting methodology it has become possible to sort leukocytes obtained from maternal blood and prepare a fraction which is relatively 'enriched' in fetal cells. To utilize these rare cells for a prenatal diagnosis of chromosome abnormalities, enrichment techniques are being improvised to make it a standard non-invasive procedure.

Fetal liver biopsy: A variety of enzymes intermediary metabolism is expressed only in the liver. The prenatal diagnosis of disorders associated with

abnormalities of this enzyme cannot be accomplished by enzyme assay of amniotic fluid or chorionic minicells. Thus, fetal liver biopsy is useful in conditions like type I glycogen storage diseases, etc.

Fetal skin biopsy: This approach is used only in those disorders where skin is involved, e.g. epidermolytic hyperkeratosis.

Preimplantation diagnosis: In this procedure one or two cells are removed from cleavage stage embryos from the patients. The embryos are identified by using molecular techniques. Subsequently, a healthy embryo is reimplanted in the uterine cavity enabling further development till full term. By doing preimplantation diagnosis, first and second trimester abortions are avoided. The couples can decide whether to attempt a pregnancy instead of aborting the fetus at a later stage thus offering minimal risk to the mother. A number of strategies developed to design optimal procedures for the preimplantation diagnosis of genetic defects are:

Polar body biopsy: The chromatin polar body is virtually "mirror image" of the chromatin of the oocyte.

Multicell biopsy: Prior to the late 8-cell stage, 1–3 blastomeres of the pre-embryo are dissociated with pipetting after boring a small hole in zona pellucida, that heals rapidly afterwards.

Blastocyst biopsy: From trophoblast (which later forms placenta) of the blastocyst a number of cells can be safely removed for analysis without adversely affecting the fetus.

Basic information required for genetic counseling: A genetic counselor must have:

1. Precise and fully confirmed diagnosis of the diseases.
2. Accurate pedigree of the family.
3. Knowledge of the mode of the inheritance of the condition.

Indications for prenatal diagnosis

1. Advanced maternal age (e.g. Down's syndrome).
2. Previous child with chromosome aberration.
3. Intrauterine growth delay.
4. Biochemical disorder.
5. Congenital anomaly.
6. Previous history of neural tube defect in the family.
7. Structural anomalies found on ultrasonography.
8. Person with mental retardation or developmental delay (e.g. fragile X syndrome).
9. Couples with a history of recurrent miscarriages.

How to identify genetic diseases**Step 1:**

1. Buildup the pedigree tree “bottom-up”, starting with the index case and ending up with grandparents, cousins, uncles, aunts, etc.
2. Ask the mother of the patient about her siblings, children, parents and all the immediate blood relatives that she can remember from her side or from her groom’s side.
3. Fill in the appropriate pedigree symbols to indicate normal, carrier, affected individuals, stillbirths, spontaneous abortions, twins, consanguinity, unknown gender, etc.

Step 2:

1. Analyze the pedigree chart and determine the mode of inheritance.
2. The negative family history should not be considered conclusive evidence against the presence of heritable condition. The presence of consanguinity does not prove recessive inheritance, it makes it more likely.

Step 3:

Calculate risk of recurrence. The perception of what constitutes “high or low” depends on the investigator. In the risk figure has two components:

1. The probability of occurrence of the disease.
2. The burden of the diseases.

Step 4:

The decision making:

1. Allow the patient or his family members to decide on continuation and termination of pregnancy.
2. Counseling should be supportive.
3. Conditions with mendelian inheritance usually have high risk of recurrence.
4. Support your conclusion with chromosomal and molecular data wherever possible.
5. Autosomal dominant condition: 50% to the offspring of the affected parents.
6. Autosomal recessive condition: 25% to the offspring of the carrier parents.
7. X-linked recessive condition: 50% risk to siblings.
8. On observing a structural chromosomal anomaly in the patient, check the parent chromosome.
9. Duplication or deletion of chromosome can result in congenital malformation or mental retardation.

Q. 17. Write about stem cells in dentistry.

Ans. Stem cells are primitive cells found in all multicellular organisms that are characterized by self-renewal and the capacity to differentiate into any mature cell type. There are 2 main types of stem cells—

embryonic stem cells and adult stem cells, which are classified according to their origin and differentiation potential.

Stem cells are cells that have the following capabilities

1. They are able to continuously produce daughter cells having the same characteristics as themselves (self-renewal).
2. They can generate daughter cells that have different, more restricted properties.
3. They can re-populate a host *in vivo* (differentiation).

Sources of stem cells: There are many potential sources for stem cells:

1. Embryonic stem (ES) cells are derived from the inner cell mass of a blastocyst from a 4 or 5 days old embryo.
2. Embryonic germ (EG) cells are collected from fetal tissue at a somewhat later stage of development (from a region called the gonadal ridge).
3. Adult stem cells that are derived from mature tissues and are found in adult tissues. They act as a repair system for the body, replenishing specialized cells, but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

Generic criteria for pluripotent embryonic stem or embryonic germ cells

1. Originate from a pluripotent cell population.
2. Maintain normal karyotype.
3. Immortal and can be propagated indefinitely in the embryonic state.
4. Clonally-derived cultures capable of spontaneous differentiation into extraembryonic tissue and somatic cells representative of all 3 embryonic germ layers in teratomas or *in vitro*.

Characteristics of mesenchymal stem cells: MSCs are described as multipotent because of their ability, even as clonally isolated cells, to exhibit the potential for differentiation into a variety of different cells/tissue lineages.

Properties of stem cells: All primate pluripotent stem cells grow in more rounded clumps with indistinct cell borders express alkaline phosphatase activity. EC cells express the tissue non-specific form and a form of the enzyme that can be detected by antibodies that react with the germ cell or placental form. The pluripotent cells require a mouse embryonic fibroblast feeder-cell layer for support. In the case of mouse ES and EG cells, this requirement can be replaced by LIF or by related members of this cytokine family, but pluripotent human EC cells, rhesus monkey ES cells, and human ES cells will not respond to LIF in such a fashion.

Recent stem cell studies in the dental field have identified many adult stem cell sources in the oral and maxillofacial region. Many types of adult stem cells reside in several mesenchymal tissues, and these cells are collectively referred to as mesenchymal stem cells or multipotent mesenchymal stromal cells (MSCs).

1. **Bone marrow mesenchymal stem cells (BMSCs) from orofacial bones:** Human BMSCs can also be isolated from orofacial (maxilla and mandible) bone marrow aspirates obtained during dental surgical procedures such as dental implant treatment, wisdom tooth extraction, extirpation of cysts and orthodontic osteotomy.
2. **Dental tissue-derived stem cells:** Stem cells have also long been assumed to exist in dental tissues because some dental tissues, such as periodontal tissues and dental pulp, can regenerate or form reparative dentin by a natural process.
 - a. **Dental pulp stem cells (DPSCs)** are cells that had phenotypic characteristics similar to those of BMSCs. MSC-like cells were subsequently also isolated from the dental pulp of human deciduous teeth (stem cells from human exfoliated deciduous teeth—SHED).
 - b. **The periodontal ligament** is another adult MSC source in dental tissues, and periodontal ligament stem cells (PDLSCs) can even be isolated from extracted teeth. PDLSCs have demonstrated the ability to regenerate periodontal tissues (cementum, periodontal ligament and alveolar bone) in experimental animal models.
 - c. MSC-like cells have also been identified in the “**developing**” dental tissues, such as the dental follicle, dental mesenchyme and apical papilla.
3. **Oral mucosa-derived stem cells**
 - a. **Oral epithelial progenitor/stem cells**, which are a subpopulation of small oral keratinocytes. Although these cells seem to be unipotential stem cells, i.e. they can only develop into epithelial cells. They may be useful for intraoral grafting.
 - b. **In the lamina propria of the gingiva**, which attaches directly to the periosteum of the underlying bone with no intervening submucosa.
4. **Periosteum-derived stem/progenitor cells:** Cultured periosteum-derived cells have been used for alveolar ridge or maxillary sinus floor augmentation. Therefore, the periosteum is a source of stem/

progenitor cells for bone regeneration, particularly for large defects.

5. **Salivary gland-derived stem cells:** Stem cells in the adult salivary gland are expected to be useful for autologous transplantation therapy in the context of tissue engineered-salivary glands or direct cell therapy.

Applications of stem cell research in dentistry

1. **Alveolar bone augmentation:** Alveolar bone regeneration by stem cells helps to regenerate the tissue. Stem cell-based therapies carry the drawbacks of high cost and labor.
2. **Tooth/root regeneration:** The ultimate goal of tooth regeneration is to develop fully functioning bio-engineered teeth that can replace lost teeth. Regeneration of the entire tooth is expected to be one of the highest achievements in the field of dentistry. Tooth engineering to form dental structures *in vivo* has been established using many different types of stem cells from mice, rats, and pigs.
3. **Mandible condyle regeneration:** Damage to the temporomandibular joint disc or condyle (condylar osteochondral defect) arising from trauma or arthritis can result in lifelong pain and disturbed masticatory function for patients. Tissue regeneration strategy on these defects can hold promise to affect the quality of life (QOL) of these patients.
4. **Tongue regeneration:** Loss of tongue tissue from surgical resection can profoundly affect the quality of life, because the tongue plays a critical role in speech, swallowing and airway protection. Therefore, reconstruction of tongue defects has been a continuing challenge in dentistry. Advances in stem cell biology and tissue engineering may enable the reconstruction of the damaged or resected tongue with normal physiological function.

Aging of mesenchymal stem cell: A number of changes occurred in physiological, functional, and molecular parameters of stem cells during long-term cultures. These changes include:

- a. Typical Hayflick phenomenon of cellular aging.
- b. Gradual decreasing proliferation potential.
- c. Telomere shortening.
- d. Impairment of functions.

The proliferative potential of MSC decreases faster after 120 days of *in vitro* expansion.



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